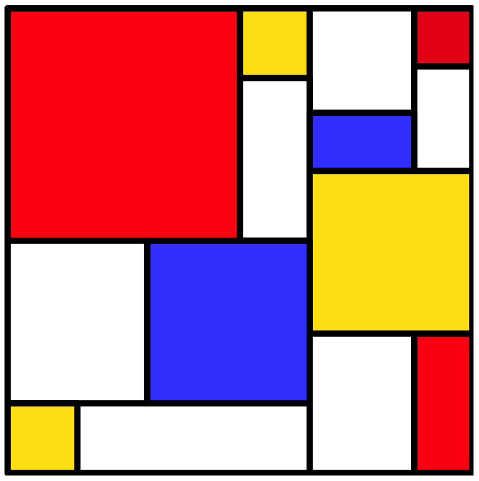
SLiM: An Evolutionary Simulation Framework

Benjamin C. Haller and Philipp W. Messer

Dept. of Biological Statistics and Computational Biology
Cornell University, Ithaca, NY 14853

Correspondence: bhaller@benhaller.com



Last revised 29 January 2019, for SLiM version 3.2.1.

Author Contributions:

SLiM 2 and later were conceived and designed by BCH and PWM, based upon the previous design of SLiM by PWM. BCH designed and implemented the Eidos scripting language, wrote almost all of the code for SLiM 2 and later (but see the acknowledgements below), and wrote this manual. PWM provided feedback and edited this manual.

Acknowledgements:

The authors want to thank Andrew Sackman, Aaron Sams, Nathan Oakes, Madeline Kwicklis, Jamal Elkhader, and all members of the Messer lab for helpful feedback and bug reports. Thanks to Kevin Thornton and Ryan Hernandez for many discussions and for their general help in promoting forward population genetic simulations. Thanks to Jared Galloway, Jerome Kelleher, and Peter Ralph for their considerable work in implementing tree-sequence recording in SLiM 3. Thanks to Simon Aeschbacher, Jorge Amaya, Bill Amos, Chenling Antelope, Jaime Ashander, Hannes Becher, Emma Berdan, Jeremy Berg, Tom Booker, Gideon Bradburd, Yoann Buoro, Deborah Charlesworth, Jeremy Van Cleve, Jean Cury, Michael DeGiorgio, A.P. Jason de Koning, Emily Dennis, Jordan Rohmeyer Dherby, Jared Galloway, Jesse Garcia, Kimberley Gilbert, Alexandre Harris, Kelley Harris, Rebecca Harris, Matthew Hartfield, Ding He, Kathryn Hodgins, Christian Huber, Melissa Jane Hubisz, Emilia Huerta-Sanchez, Jacob Malte Jensen, Peter Keightley, Jerome Kelleher, Andy Kern, Bhavin Khatri, Bernard Kim, Athanasios Kousathanas, Chris Kyriazis, Benjamin Laenen, Áki Láruson, Stefan Laurent, Eugenio Lopez, Kathleen Lotterhos, Andrew Marderstein, Sebastian Matuszewski, Mikhail Matz, Rupert Mazzucco, Maéva Mollion, Miguel Navascués, Dominic Nelson, Bruno Nevado, Etsuko Nonaka, Greg Owens, Harvinder Pawar, Martin Petr, Denis Pierron, Fernando Racimo, Peter Ralph, David Rinker, Murillo Fernando Rodrigues, Andrew Sackman, Kieran Samuk, Derek Setter, Onuralp Söylemez, Stefan Strütt, Rob Unckless, Christos Vlachos, Silu Wang, Aaron Wolf, Yan Wong, and Justin Yeh for comments and feedback that has led to improvements in SLiM. Thanks also to everyone on stackoverflow, an invaluable resource and a great community. Finally, we want to thank Dmitri Petrov, whose support was instrumental in the initial conception of SLiM.

Citation:

To cite **SLiM 3** in a publication, please cite:

Haller, B.C., and Messer, P.W. (2017). SLiM 2: Flexible, interactive forward genetic simulations. *Molecular Biology and Evolution* (early access). DOI: https://doi.org/10.1093/molbev/msy228

Papers using **tree-sequence recording** should perhaps also cite that paper:

Haller, B.C., Galloway, J., Kelleher, J., Messer, P.W., & Ralph, P.L. (2018). Tree−sequence recording in SLiM opens new horizons for forward−time simulation of whole genomes. *Molecular Ecology Resources* (early access). DOI: https://doi.org/10.1111/1755-0998.12968

Papers which only use **SLiM 2** can still cite that paper:

Haller, B.C., and Messer, P.W. (2017). SLiM 2: Flexible, interactive forward genetic simulations. *Molecular Biology and Evolution 34*(1), 230–240. DOI: http://dx.doi.org/10.1093/molbev/msw211

Papers which wish to cite **this manual** (perhaps because they make reference to a recipe) should cite:

Haller, B.C., and Messer, P.W. (2016). SLiM: An Evolutionary Simulation Framework.
URL: http://benhaller.com/slim/SLiM_Manual.pdf

And if you wish to cite a publication about **Eidos**, please cite the Eidos manual:

Haller, B.C. (2016). Eidos: A Simple Scripting Language.
URL: http://benhaller.com/slim/Eidos_Manual.pdf

URL:

http://messerlab.org/slim

License:

Disclaimer:

Contents

PART I: THE SLiM COOKBOOK

Part I: The SLiM Cookbook

1. SLiM overview

1.1 Introduction

SLiM is an evolutionary simulation package that provides facilities for very easily and quickly constructing genetically explicit individual-based evolutionary models. By default, SLiM is based upon a Wright-Fisher or "WF" model of evolution; in particular, (1) generations are non-overlapping and discrete, (2) the probability of an individual being chosen as a parent for a child in the next generation is proportional to the individual's fitness, (3) individuals are diploid, and (4) offspring are generated by recombination of parental chromosomes with the addition of new mutations. Some of these assumptions can be relaxed in WF models using techniques described in this manual, and an alternative non-Wright-Fisher or "nonWF" type of model can even be used instead; nevertheless, the default WF model is the conceptual foundation of SLiM, and it should be understood thoroughly before venturing into more advanced models.

The original version of SLiM (through version 1.8; Messer 2013) was written by Philipp Messer, now of Cornell University; its name stands for **S**election on **Li**nked **M**utations. SLiM 2 and later – the subject of this manual, hereafter simply referred to as SLiM – is a ground-up redesign of SLiM (by Benjamin C. Haller, now of the Messer Lab at Cornell) that provides much greater power, flexibility, and speed on top of the same foundational architecture as the original.

SLiM is based upon two main components: a simple scripting language called Eidos that was invented for use with SLiM, and a set of Eidos classes that implement entities such as subpopulations, mutations, and chromosomes. A minimal SLiM simulation, such as you will see in section 4.1, comprises just a few lines of Eidos code; virtually all of the simulation details are handled by SLiM, so the Eidos script needs only to set up basic parameters such as the population size and mutation rate. Because of the extensibility provided by Eidos, however, it is straightforward to extend such a simulation to model almost any scenario.

Regardless of the specific problem studied, evolutionary simulations will often entail common design elements: multiple subpopulations connected by migration, for example, or selective sweeps, or spatial and temporal variation in selection. Such design elements will come up over and over for users of SLiM, and it might not be obvious – particularly to biologists with little programming experience – how to model them using the toolbox provided by Eidos and SLiM. The first part of this manual has thus been structured as a "cookbook", an assemblage of recipes showing how to build different sorts of models in SLiM. The design of each recipe will be explained, so that users of SLiM feel comfortable modifying the recipes to build their own models.

Under the hood, SLiM is a complex piece of software, with dozens of source files devoted to implementing both the Eidos language and the Eidos classes provided by SLiM. However, users of SLiM should not need to confront that complexity; SLiM users should literally never need to delve into the C++ and Objective-C code that drives SLiM. All that you need to understand, as an end user, is the Eidos scripting interface that SLiM presents for your use. Understanding the Eidos language itself is an important part of using SLiM effectively; this manual will briefly introduce Eidos concepts as they arise, but for a more thorough and complete introduction to Eidos it is recommended that you refer to its separate manual (Haller 2016). Eidos is similar to the popular R language (R Core Team 2015); if you have used R, Eidos should feel natural. (The Eidos manual discusses why we invented a new language for SLiM, rather than using an existing language.)

This manual does not need to be read from cover to cover; each recipe is designed to stand alone, so if you are interested in a specific problem – how to model epistasis in SLiM, say – it may be possible to turn directly to that recipe. However, concepts do build on each other, and a familiarity with Eidos also builds through the course of this manual. We recommend that all SLiM users read at least this introductory chapter, which lays out the conceptual foundations of SLiM.

1.2 Why SLiM?

Many evolutionary simulation packages already exist, from custom-built one-off models that address only a single problem, to simulation toolkits designed to fit a wide variety of tasks. It would be reasonable to ask why we have made yet another toolkit, and what sets SLiM apart. This section will explain what SLiM is designed to do and why it adds something important and unique to existing modeling tools. Note that here we are discussing SLiM 2 and later, which is quite different in its design philosophy and approach than earlier versions of SLiM.

The primary reason for SLiM is flexibility. Most evolutionary modeling toolkits, including SLiM 1.8, are quite limited in their abilities. They are not easily extensible or modifiable; typically, if you wish to make such a toolkit do something new, you need to modify the actual source code (often C or C++) in which the toolkit is written – a non-trivial task. Some toolkits embrace this shortcoming as a feature, and are thus designed as a set of C++ templates or other reusable objects; but again, although this approach is flexible, a great deal of programming experience is needed. Because existing toolkits are so difficult to modify and extend, it is often simpler for researchers to write their own purpose-built model from scratch; however, this also entails substantial drawbacks. First, it involves reinventing the wheel over and over. Second, it limits the level of complexity attainable, since each research project begins again more or less from scratch. Third, it is a very bug-prone approach, since the code underlying such simulations is often complex, and all of the debugging and testing that went into previous models is lost with each new model. SLiM is designed to radically simplify the process of making an evolutionary model, because of the way that the inner mechanisms of the SLiM simulation are exposed in the Eidos scripting language. Modifying a simulation to add a new and complex behavior such as epistasis or sequential mate choice can often be expressed in just a couple of lines of simple Eidos code – a much simpler proposition than trying to do the same thing in the underlying C++ in which the toolkit is written. The underlying SLiM engine is quite complex – it contains a full interpreter for the Eidos language – but it can be treated as a black box, and never needs to be modified or understood by the end user at all. The script that drives a particular simulation, on the other hand, can usually be trivially short, easily understood, and quickly modified. The end result is immense power and flexibility coupled with immense simplicity and reusability.

A second reason for SLiM's existence is performance. When writing a one-off model, it is often prohibitive – in terms of both time and effort – to optimize the model for fast execution, and once code is optimized it becomes much harder to maintain and modify, hindering reusability. Because SLiM will be used for many different models, however, we deemed it worthwhile to spend the effort on optimization. Months of hard work have gone into making SLiM run fast, including a number of complex and non-obvious algorithmic optimizations. By using SLiM, you get all of the speed benefits of those optimizations for free. Individual-based simulations are often speed-limited; one is often forced to explore only a limited range of parameter space, or use smaller population sizes than desired, or make other such compromises because of limited computing resources. SLiM helps to lift that constraint.

A third reason for SLiM's existence is to provide interactive execution and graphical debugging. With SLiMgui on OS X, you can visualize your simulation as it runs, with graphical depictions of mutations, genomic elements, subpopulations, migration patterns, and simulation metrics. You can single-step through your simulations, examine the values of all of the underlying objects, and even execute arbitrary Eidos code to modify your simulation as it runs. This allows much more rapid and bug-free simulation development. We highly recommend that you use SLiMgui on OS X for development even if your production runs will be on Linux or elsewhere; the value of graphical model development and debugging is immense (Grimm 2002).

We believe that flexibility, performance, and graphical interactivity make SLiM a worthy addition to the ecosystem of evolutionary modeling toolkits. We hope that you will agree.

1.3 A quick summary of SLiM

This section is a quick summary of SLiM's design, as a brief introduction to provide context for the recipes in this cookbook. See part II of this manual, the SLiM Reference, for further details.

Glossary. We begin with a glossary of terms that have a special meaning in SLiM:

simulation: The *simulation* in SLiM is the top-level Eidos object, of class `SLiMSim`, corresponding to the running simulation model. All other objects defined by SLiM are contained within the simulation object.

population: The *population* in SLiM comprises all of the individuals being simulated by SLiM. There is no Eidos object corresponding to the population; the simulation object handles everything related to the population.

subpopulation: The population is divided into *subpopulations*, discrete groups of individuals which may or may not be connected to each other by migration. The Eidos class `Subpopulation` is used to represent the subpopulations in a simulation.

individual: An *individual*, in SLiM, is a diploid organism composed of two haploid *genomes* (see below). Individuals are represented by the Eidos class `Individual`. The individual is the conceptual level at which fitness is computed, mate choice is conducted, and so forth.

genome: A *genome* is the haploid set of all mutations occurring in the genetic material represented by the genome object. Each individual contains two genomes, representing the two homologous chromosomes of the individual. The Eidos class `Genome` is used to represent genomes.

mutation: A *mutation* is a change in the genetic information of an individual, represented by the Eidos class `Mutation`. Mutations have a defined position in the genome, a selection coefficient, and information about when and where they arose. Each mutation references a *mutation type* (see below) that governs some additional properties of the mutation, such as its dominance coefficient.

mutation type: Mutations are drawn from a particular *mutation type*, representing simulation-dependent categories of mutations (neutral, beneficial, lethal, synonymous, etc.). In general, the mutation type determines the distribution of fitness effects (DFE) from which mutations of that mutation type are drawn. The mutation type also determines the dominance coefficient of all mutations of that type. The Eidos class `MutationType` is used to represent mutation types in SLiM.

chromosome: In SLiM's terminology, the *chromosome* is the positional map of regions, such as genes, being modeled by SLiM; the term does *not* refer to a single chromosome carried by a particular individual (the term *genome* is used for that purpose). The chromosome, represented by the Eidos class `Chromosome`, defines regions according to both their recombination rate and their mutational profile.

genomic element: The chromosome is spanned by non-overlapping *genomic elements*, of Eidos class `GenomicElement`, each referencing a *genomic element type* (see below).

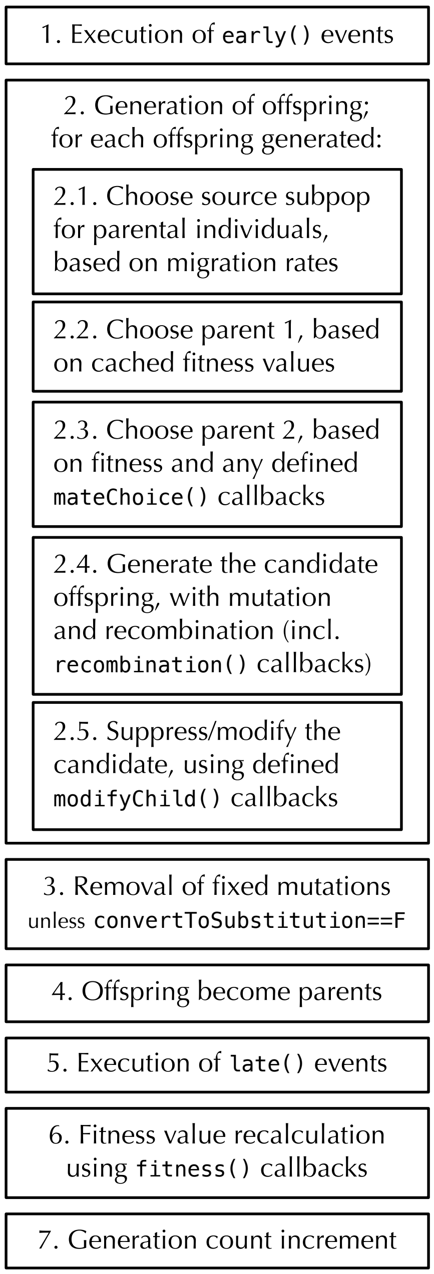
genomic element type: A *genomic element type* defines the particular mutation types that can occur in genomic elements of the given type. It is represented by Eidos class `GenomicElementType`. Biological examples of genomic element types could be introns, exons, or non-coding regions. All of the genomic elements referencing a type use that type's mutational profile.

substitution: When mutations reach fixation in the entire population, they are generally replaced by substitution objects, of Eidos class `Substitution`, for efficiency reasons. The substitution provides a permanent record of the fixed mutation's characteristics.

Population structure. SLiM allows arbitrary population structure; any number of subpopulations may exist, connected by any pattern of migration, and subpopulations may come into existence, change size, and be removed at any time. Mate choice occurs within subpopulations; adult organisms do not migrate or mate between subpopulations. Migration occurs at the juvenile stage. Individuals in SLiM are always diploid, and gametes are always haploid; at present, SLIM does not support other ploidy levels (but haploids can be modeled with scripting; see the recipe in section 13.13). These topics are discussed further in chapter 5.

Sexual reproduction. SLiM can model either hermaphroditic individuals (no distinction between sexes) or sexual individuals (distinct males and females). In either case, individuals normally undergo biparental mating to produce offspring through sexual recombination (including both crossing over and, optionally, gene conversion). Clonal reproduction is also supported instead of or in addition to biparental mating, and in the hermaphroditic case, SLiM also supports self-fertilization. When modeling sexual individuals, the sex ratio is controllable, and sex chromosomes may be modeled. These topics are discussed further in chapter 6.

The sequence of events within one generation in WF models.


1. Execution of `early()` events
2. Generation of offspring; for each offspring generated:
2.1. Choose source subpop for parental individuals, based on migration rates
2.2. Choose parent 1, based on cached fitness values
2.3. Choose parent 2, based on fitness and any defined `mateChoice()` callbacks
2.4. Generate the candidate offspring, with mutation and recombination (incl. `recombination()` callbacks)
2.5. Suppress/modify the candidate, using defined `modifyChild()` callbacks
3. Removal of fixed mutations unless `convertToSubstitution==F`
4. Offspring become parents
5. Execution of `late()` events
6. Fitness value recalculation using `fitness()` callbacks
7. Generation count increment

Genetics. SLiM is genetically explicit in the sense that it models mutations at specific base positions in genomes with an explicit chromosome structure; SLiM does not, however, model nucleotide sequences (but see section 13.12). The chromosome modeled by SLiM is composed of genomic elements (e.g., sections of a gene), each of a particular genomic element type (e.g., intron versus exon). The genomic element type defines the mutational profile of elements of that type, using a set of mutation types and associated probabilities. These topics are discussed further in chapter 7.

Fitness. By default, SLiM calculates fitness multiplicatively, based upon all of the mutations possessed by each individual. The selection coefficient *s* of a given mutation defines the mutation's fitness effect when homozygous (1+*s*); when heterozygous, the fitness effect is modified by a dominance coefficient *h* (1+*hs*). The fitness effects of mutations may be altered by `fitness()` callbacks that provide full control over how the fitness of an individual is calculated given the particular set of mutations present in its genome, and possibly other properties of the population. These topics are discussed further in chapter 9.

Life cycle. SLiM is based, by default, on an extended Wright-Fisher or "WF" model with non-overlapping, discrete generations (a non-Wright-Fisher or "nonWF" model can also be used, as discussed in section 1.6 and chapters 15 and 20, but that is an advanced topic that we will pass over here). Within each generation, events occur in a fixed order (see left). Each generation begins with the execution of user-defined Eidos scripts called `early()` events. Examples of `early()` events might be demographic events, such as changes in population size, population splits, changes in migration rates, etc. Offspring are then generated by drawing gametes from the parent population according to fitness; this default mating scheme may be modified to implement non-standard mating scenarios via user-defined `mateChoice()` callbacks (see chapter 11). Gametes are generated from the genomes of the candidate parents, modified by mutation and recombination; the standard user-defined recombination map can be modified arbitrarily for each gamete generated using a `recombination()` callback (see sections 13.5 and 21.5). After offspring have been created, their genomes can be modified according to user-defined rules using `modifyChild()` callbacks (see chapter 12). After (optional) removal of fixed mutations from the model, the offspring become the parents. Next is another opportunity for Eidos events – in this case, `late()` events – to run. This is where output events, such as drawing a random sample of individuals from the populations, would typically be specified. Fitness values are then calculated, modified by `fitness()` callbacks (see chapter 9). Finally, the simulation advances to the next generation.

Tags. User-defined "tag" values can be attached to almost all of the objects defined by SLiM in order to associate your own information with SLiM's objects, whether short-term flags or long-term state. Tags are used in the recipes in sections 9.4.3, 9.4.4, 10.5.2, 12.1, 13.1, and 13.3, which provide a variety of examples of their utility. In SLiM 2.2, a dictionary-like `getValue()` / `setValue()` mechanism was added to the `Individual`, `SLiMSim`, and `Subpopulation` classes (and in SLiM 2.4, now `MutationType`, `GenomicElementType` and `InteractionType` too; and in SLiM 2.5, `Mutation` also; and in SLiM 3.0, `Substitution` also). This facility provides an even broader and more flexible way to attach model state to those objects; see the class references in chapter 21 for details on these functions, and see the recipe in section 11.1 for an example of their use.

Continuous space. Beginning in SLiM 2.3, SLiM adds support for continuous space. If this optional feature is enabled, individuals in SLiM maintain a spatial position – either (*x*), (*x*, *y*), or (*x*, *y*, *z*) – within their subpopulation. These spatial positions can be changed at any time (simulating phenomena such as foraging and migration, for example), and are used to create a spatial visualization of the subpopulation in SLiMgui. Positions can used in script in any way, allowing models to incorporate a concept of continuous space in any way desired. In particular, spatial positions may be used as the basis for spatial interactions between individuals (see below), and may be used in conjunction with spatial maps that define variation in environmental variables across continuous space. This advanced feature is first introduced in recipes in chapter 14.

Interactions. Beginning in SLiM 2.3, SLiM adds a new class, `InteractionType`, which can govern interactions between individuals. Interactions can still be handled with pure Eidos code, but the use of `InteractionType` automates and accelerates many common tasks, such as finding the total interaction strength felt by an individual (as a result of competition, for example). `InteractionType` can also manage spatial interactions, providing features such as interaction strengths that vary according to distance, and handling spatial queries such as nearest-neighbor searches. This advanced feature is first introduced in recipes in chapter 14.

Section 1.4 sketches out some practical details of how SLiM is typically used. Section 1.5 provides a more detailed overview of some of the concepts above. Section 1.6 then introduces non-Wright-Fisher or "nonWF" models, and section 1.7 introduces tree-sequence recording; these are both advanced topics, but it is good to be aware of the existence of these features and the reasons why you might wish to use them. Chapter 2 provides instructions on building and installing SLiM on various platforms. Chapter 3 gives an introduction to SLiMgui, the graphical modeling environment provided for use on Mac OS X. The remainder of Part I of this manual, the SLiM Cookbook, then provides "recipes" demonstrating the core concepts of SLiM. Part II of this manual, the SLiM Reference, provides technical reference documentation for SLiM, including such aspects as the generation cycle, the Eidos classes provided by SLiM, the various types of events and callbacks, and the output formats supported by SLiM, beginning in chapter 19.

1.4 The typical SLiM usage pattern

Before delving more deeply into the concepts introduced in the previous section, it might be helpful to clarify how a typical user would use SLiM, in practical terms.

First of all, many or most users will use the SLiMgui modeling environment on Mac OS X for their model development and testing, and perhaps for exploratory, non-production runs as well. SLiMgui provides many tools for model development, such as code completion, syntax coloring, online documentation, interactive model execution, and graphical debugging. It also makes model development logistically simpler; there is no need to write a dispatch script, no need to execute Unix commands in a terminal, etc. When learning how to use SLiM, it is therefore strongly recommended that you find a Mac and use SLiMgui. Note that all of the recipes in this manual are directly accessible in SLiMgui through the Open Recipe submenu of the File menu.

Second, many or most SLiM users will do their "production" model runs on a computing cluster. One reason is that individual-based models often take a long time to execute; SLiM is highly optimized, but simulating the genomic details of a large number of individuals over many generations is inevitably slow. Another reason is that many replicate runs are typically needed; one run of an individual-based model provides just one data point, one solitary example of what *could* happen, so one usually needs to perform many runs and then use statistical methods to draw inferences (just as one often would in field-based or lab-based research). Finally, most studies involving individual-based modeling explore a "parameter space", examining how the model's outcome depends upon the parameters of the model; each set of parameter values explored implies another full set of replicated runs. Together, these facts mean that a single study using SLiM might entail many years of processor time; a computing cluster is thus often needed.

For this reason, SLiM is designed to fully utilize a single processor; it is not designed to take advantage of multiple processors using multithreading or MPI. A single run of the `slim` command runs a given model a single time; to conduct the many runs that are typically needed, `slim` will be run many times. This single-threaded design makes it straightforward for the user to run a separate instance of a model on each processor on a multicore machine or a computing cluster. This can be done manually in some cases, but is more typically done using a batch-queueing system such as Open Grid Scheduler. Either way, some sort of a dispatch script is generally needed to schedule each of the individual runs of `slim`. Because there are so many different possible ways that the user might want to run SLiM, and so many different computing environments in which it might be run, such a dispatch script is not provided as a part of the SLiM package; you will need to write your own. However, this is usually extremely straightforward. It can usually be done in whatever scripting language you prefer, from R or Python to a Bash shell script, and often just consists of a loop over all of the parameter values and replicates desired, with a call to launch or schedule a run of `slim` inside that loop. In Python, sublaunching a Unix process can be done with the `subprocess` package; in R, with `system()` or `system2()`; in a Bash shell script, by just invoking `slim` directly. If you are working on an institutional computing cluster, the cluster administrator may be able to provide you with examples of dispatch scripts appropriate for that environment.

Finally, SLiM users will typically want to collect results from model runs and perform statistics and other analyses on them. This can sometimes be done directly in the dispatch script; that script might collect the model output and tabulate simple results as runs complete. In other cases, each invocation of slim will be set up to produce its own output files, and then a separate analysis script – typically written in a language like R or Python that has support for statistics and plotting – will read in those output files, parse the relevant information out of them, and conduct the desired analyses. In this undertaking, you are on your own. However, it is worth noting that SLiM can generate output in some standard file formats, such as VCF and MS, and that many tools already exist to read in and analyze such standard-format files, so in some cases you might be able to use pre-existing software for at least some of your analysis. If your model uses tree-sequence recording (see section 1.7), you can also output a `.trees` file that can be read and processed in Python using the `msprime` package, making many types of post-run analysis much easier (see examples in chapter 16); indeed, this could in itself be a compelling reason to use tree-sequence recording, since parsing output files is otherwise such an annoyance. Finally, in some cases you might want to do some of the needed analysis inside the SLiM model, in Eidos code, to simplify the post-processing needed. For example, if your analysis needs the number of mutations fixed at the end of each model run, it might be simpler to count the fixed mutations inside the SLiM model, and just output that count, than to parsing full genomic output files from each model run just to extract the count of fixed mutations. It will be beneficial to think, up front, about how to design your model and your analysis code so that they communicate as cleanly and simply as possible.

1.5 Conceptual overview

This section will delve into further detail on some of the concepts set out in section 1.3 (which should be read before this section), to present a more complete picture of how SLiM works at a conceptual level. We will not show any Eidos code here; that will be left for the recipes in the "cookbook" that begins in chapter 4. We will, however, make reference to the Eidos classes used by SLiM to represent various concepts, and to some of the properties and methods of those classes. We will gloss over some minor details here in order to present the big picture as clearly as possible; for more comprehensive information, see the SLiM Reference that begins in chapter 19.

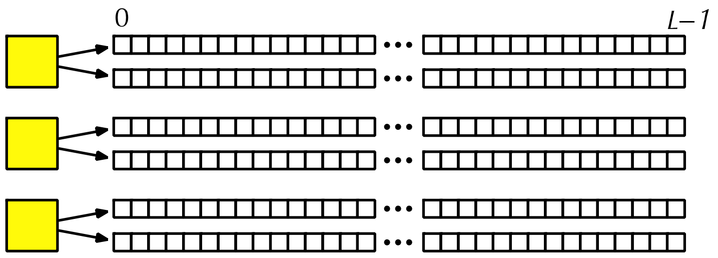
1.5.1 Individuals and genomes

SLiM is a framework for running individual-based models; this means that every individual organism in the model is simulated explicitly. Each individual is represented in SLiM as an instance of the `Individual` class in the Eidos scripting language (see section 21.6). At the most minimal level individuals are born and die, and in between they find mates and produce offspring (or they reproduce by selfing or cloning); these actions are built into SLiM. If optional extensions to SLiM are enabled (using the `initializeSLiMOptions()` function; see section 21.1), SLiM can also keep some pedigree information regarding individuals (up to the grandparental level), and can keep track of the spatial positions of individuals on a landscape. In more complex models individuals may also do things like gather resources, learn things, interact with other individuals, be subject to events that alter their state, and exhibit behavior; these actions are not built into SLiM, but may easily be implemented in Eidos script.

Perhaps most importantly, since SLiM models genetically explicit simulations, individuals contain genetic information. Individuals in SLiM are diploid; each individual thus possesses two homologous chromosomes (or one X and one Y chromosome, if sex chromosomes are being simulated), referred to as the *genomes* of that individual. (It is possible to model more than one chromosome in SLiM, conceptually, but this is done by using a recombination map that specifies free recombination at particular positions, effectively subdividing the chromosome into unlinked sub-chromosomes; see, e.g., section 13.1.) Each of the two genomes of an individual is represented using an instance of the `Genome` class in Eidos (see section 21.3).

A genome is essentially a container that holds a set of mutations. If both of an individual's genomes contain exactly the same mutation (a surprisingly subtle concept, which will be defined rigorously in the next subsection), the individual is homozygous for that mutation; if a given mutation is contained in only one of the two genomes, the individual is heterozygous for that mutation. Note that SLiM does not model nucleotides explicitly (although it is possible to layer a concept of nucleotides on top of SLiM, in script; see section 13.12), but it does model explicit, discrete base positions along the genome.

The overall picture, then, looks like this:



Each yellow square represents one individual. Each individual contains two genomes; and each genome contains the state of all of the base positions along the chromosome, from beginning (position 0) to end (position *L*−1, so that the chromosome is of length *L*). Each base position is represented here as an empty box, and all of the boxes from 0 to *L*−1 together represent a genome.

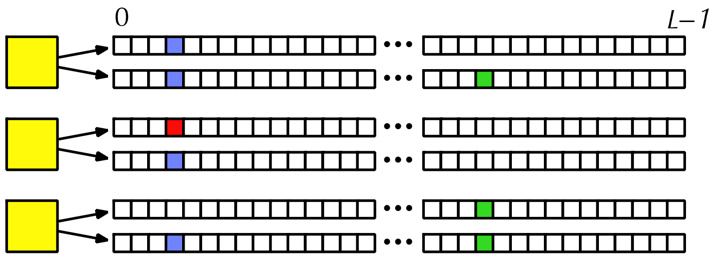
A key concept in SLiM is that genomes begin, by default, as empty: they contain no mutations and no genetic information. This can be thought of as the "wild type", in a sense, and we will refer it to in that way sometimes in what follows, but it does not have to represent the wild-type state of the organism you are modeling. Instead, it simply represents the base, un-mutated state of individuals, whatever you want to consider that to be. All mutations in SLiM can be thought of as modifications that are layered on top of this empty base state. The base state can also be thought of as "neutral", in terms of fitness, but it does not have to actually be neutral (i.e., `1.0`) in absolute fitness. Instead, the base state can have any absolute fitness value you like – but in general that is unimportant, since SLiM's core engine is only concerned with relative fitness (in WF models, the default mode of operation, which we will limit ourselves to in this discussion). When the simulation begins, and all genomes are empty, it does not matter to SLiM what the absolute fitness of those empty genomes is; since they all have the *same* absolute fitness, they all have a *relative* fitness of `1.0`, and that is what matters to SLiM. The fitness effects of mutations then modify those relative fitnesses, multiplicatively.

You can, of course, set up your simulation to begin with whatever mutational state you want; even more commonly, a simulation will begin with a "burn-in" period that establishes an equilibrium level of genetic diversity through mutation–selection–migration balance before the more interesting part of the simulation begins. It is important to understand that such genetic diversity is always built on top of empty chromosomes in SLiM, however. In general, if two mutations are segregating at a given base position, there are effectively *three* alleles in the population at that base position: the first mutation, the second mutation, and what you could think of as the "wild-type allele" represented by the *absence* of either of those mutations. In script, you could force a mutation to exist at every base position in every genome, so that there are no empty positions in any of the genomes in your simulation; if you do so, however, you will find that your simulation then runs quite slowly, since SLiM is having to track and manage all of those mutations, so such a strategy is usually undesirable.

Learning to let go of the idea of chromosomes filled with genetic information at every position (as would be the case in a nucleotide-based model) and think instead in terms of mutations layered on top of the empty "wild-type" state is an essential conceptual leap to make in using SLiM. To move from one conceptual model to the other, imagine the "wild-type" nucleotide sequence for your study organism: some specified sequence of A, T, G, and C. Whatever that sequence might be, it is represented in SLiM by the absence of any genetic information at all: empty chromosomes. SLiM tracks only mutations on top of that sequence: SNPs, in the nucleotide-based paradigm. But any individual that does not possess a SNP at a given location instead possesses the "wild-type" nucleotide, conceptually – represented in SLiM by an empty base position.

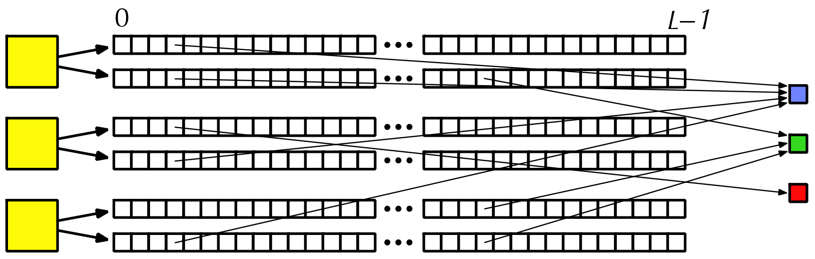
1.5.2 Mutations and substitutions

With the foundation of individuals and genomes laid by the previous section, let's now explore the idea of mutations in SLiM in more detail. In SLiM, a mutation is an instance of class `Mutation` in Eidos (see section 21.8). A mutation has various properties – its base position and its selection coefficient, most importantly. In SLiM, the multiplicative fitness effect of a mutation with selection coefficient *s* is 1+*s* for a homozygote; in a heterozygote it is 1+*hs*, where *h* is the dominance coefficient (kept by the mutation type; see section 1.5.4). Let's update our conceptual schematic to include some mutations:



This simulation has three mutations, represented here with blue, red, and green. At position 3, the first individual is homozygous for the blue mutation, the second individual is heterozygous for red and heterozygous for blue, and the third individual is heterozygous for blue (the other allele in that individual being the empty "wild-type allele" as discussed above).

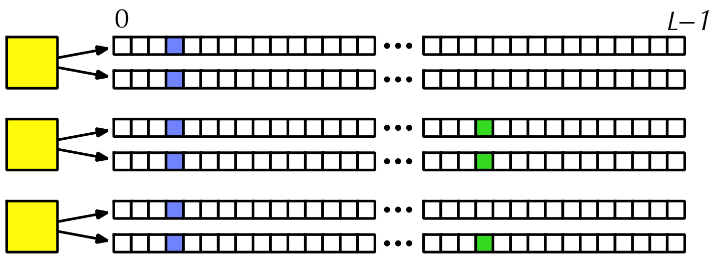
An important concept to absorb is that the genomes that contain the blue mutation do not just contain their own particular copies of blue-mutation-type information; they actually contain *references* to the very same shared blue-mutation object. A more accurate conceptual diagram might therefore look like this:



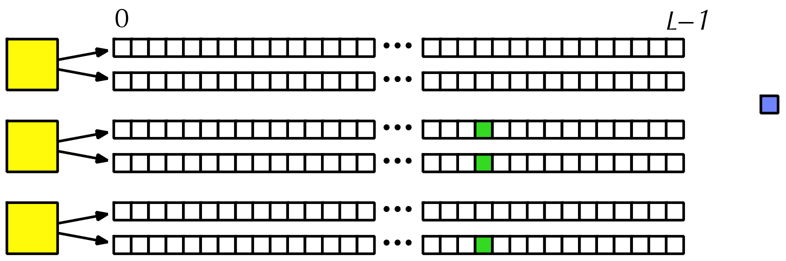
Since that is quite difficult to interpret visually, we will stick with showing mutations as residing inside genomes; but you should always keep in mind that mutations are really shared objects. A new mutation object is created either (1) when a random mutation event occurs in SLiM (as governed by the overall mutation rate set for the simulation), or (2) when requested by the simulation script with the `addNewMutation()` or `addNewDrawnMutation()` methods of `Genome` (see section 21.3.2). In both cases, *these events always create a new mutation object*, even if a mutation with exactly the same properties – position, selection coefficient, etc. – already exists in SLiM. In our conceptual diagram above, the blue and red mutations might be identical in every detail; they are nevertheless considered to be different mutations by SLiM, and will be tracked separately and never merged into a single identity. You can think of this as representing a mutational lineage, a sort of identity by descent; the red and blue mutations might represent the very same SNP, but they arose due to separate mutational events, and thus they seeded separate mutational lineages.

This distinction becomes particularly important when you ask whether two genomes contain "the same mutation" – if you ask, for example, whether a given individual is heterozygous or homozygous for a given mutation. The second individual in the diagram is heterozygous for blue and heterozygous for red; even if the blue and red mutations are identical, the individual is not considered by SLiM to be homozygous. If the fitness effects of these mutations entail a dominance effect, this could be important – the fitness effect of being red/blue would then be different from the fitness effect of being red/red or blue/blue. Often this can be ignored; if mutations are neutral then dominance doesn't matter, and if mutational effects are drawn from a distribution of fitness effects then in general no two new mutations will be the same anyway. However, if some mutations in a simulation use a fixed, non-neutral fitness effect with dominance then this might become important; this could be important in some soft-sweep models, for example. In such cases, you may wish to ensure that all references to identical mutations are transmuted into references to the same object, maintaining a single mutation for all lineages (see, e.g., section 13.12). When new mutations are being introduced in script, rather than by SLiM, you can ensure that an existing mutation object is used by using the `addMutations()` method of `Genome` (see section 21.3.2), which adds already existing mutations to a genome instead of creating new mutation objects (and thereby new mutational lineages).

Another key concept involving mutations is that by default, mutations are removed from the simulation when they become fixed. Suppose that, after mate choice and biparental mating, the next generation of our conceptual diagram looked like this:

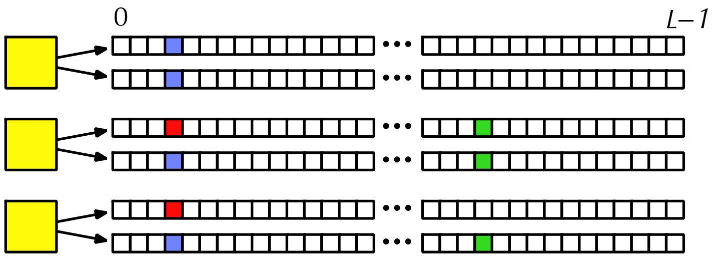


This state will never be visible to the simulation script, because at the end of offspring generation it will be replaced by this state instead:



The fixed mutation has been removed from the simulation and stored as a "substitution" object (represented here by the blue square to the right). This substitution object will be kept by SLiM forever, to remember the fixed mutation, and this substitution object is available to the script; but the mutation is no longer contained by the genomes of each individual, and it no longer influences SLiM's fitness computations. This is usually a good idea, because it allows SLiM to run much faster than it otherwise would; without removal of fixed mutations, simulations would slowly bog down under the weight of more and more accumulated fixed mutations. It is also usually safe, since a mutation that is possessed by every individual will usually have an effect on *absolute* fitness but not on *relative* fitness – since its multiplicative fitness effect is the same in every individual, it can be neglected. However, simulations that involve epistasis, or that otherwise depend upon mutations in ways that go beyond their direct effect on relative fitness, may wish to disable this automatic conversion for the mutations involved in such effects; this can be done easily in SLiM using the `convertToSubstitution` property (see section 21.9.1).

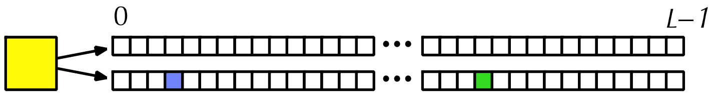
The above ideas, about the distinct identity of each mutational lineage and the way that fixation is defined in SLiM, combine in a way that is worth mentioning since it might be unexpected. Suppose that there are two mutations, blue and red, segregating at base position 3, as above, and suppose further that these mutations are identical in every detail but arose separately, as described above. Finally, suppose that the population reaches this state:



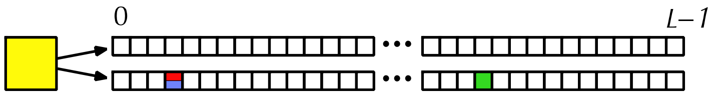
It might be natural to suppose that the mutations at position 3 would be considered to have fixed, and would be removed, as above, given that they are all identical and merely represent independent mutational lineages of what you might think to be the same mutation. As above, however, this is not how SLiM thinks! Since the blue and red mutations are different mutation objects, neither is considered to have reached fixation; fixation in SLiM occurs when a specific mutation reaches a frequency of `1.0`, without any consideration for other identical mutations segregating in the population. In a scenario like this, such as a soft-sweep model, if you want fixation of independent mutational lineages to be detected you will need to either merge the independent lineages yourself in script, as described above, or simply detect fixation yourself directly. You could detect fixation by checking that every genome in the model contains an appropriate mutation (either red or blue, in this case), or by summing the counts of all of the appropriate mutations in the population to confirm that the total count is equal to 2*N* (where *N* is the population size and the constant factor of 2 accounts for diploidy). (You might be inclined to sum the mutation frequencies instead and compare to `1.0`, but this strategy is vulnerable to floating-point roundoff error, so it is not advisable.) This is all simpler than it sounds; the soft-sweep recipes in sections 10.5 provide some examples of this.

1.5.3 Mutation stacking

There is one more key concept about mutations in SLiM to consider, and it is this: by default, a given base position in a given genome may actually contain more than one mutation – indeed, it may contain an arbitrarily large number of mutations. This is referred to as “mutation stacking”; the multiple mutations at a single base position in a given genome are referred to as being “stacked”. For example, imagine that this individual exists in a SLiM simulation:

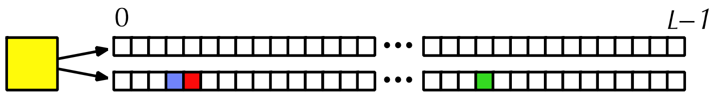


And then imagine that a new mutation, which we will show as red, occurs at the same position, in the same genome, where the blue mutation already exists. By default, here is what will happen:



The red mutation has stacked on top of the blue mutation; both mutations now exist at that position in that genome. This does not fit terribly well into the concept of “genotype” – SLiM does not really think in terms of genotypes. You could perhaps say that the genotype of this individual is something like “wild/red-blue”, if you wished, where “red-blue” is the allele created by the stacking of a red and a blue mutation together at the same locus. SLiM, however, just thinks in terms of the mutations actually possessed by each genome, so in SLiM's terms, rather than talking about genotype, we would simply say that the individual is wild-type (i.e., empty) at the given position in one genome and has a red mutation and a blue mutation at that position in the other genome. We could also say that the individual is heterozygous for red and heterozygous for blue; that is true, but is a bit ambiguous since the same would be said of a red/blue heterozygote that had a red allele in one genome and a blue allele in the other; unless the red and blue mutations are epistatic, however, that distinction is probably unimportant. Note that further mutations at the same position could occur as well, and would stack on top of those already present, making all this even more complex. Probably the simplest thing is to learn to think in the same terms in which SLiM thinks: which mutations are present in which genomes.

This behavior of SLiM is perhaps quirky, but usually harmless. It is not common for mutations to end up stacked in practice, since normal mutation–selection balance in finite populations usually clears out genetic diversity quickly enough that it is unusual for a new mutation to occur right on top of another mutation that is still segregating in the population. Furthermore, when mutations do occasionally stack, it is usually not important to the dynamics of the model; in most cases the resulting behavior is identical, for practical purposes, to if the new mutation had occurred at an immediately adjacent base position instead, which would result in the two mutations being extremely tightly physically linked rather than actually being stacked:



In principle these mutations could be separated by recombination, whereas the stacked mutations cannot be, but in practice that is unlikely enough that it will probably not make a difference to the model's dynamics. It is therefore important to understand that SLiM works in this way, but in most cases models do not need to concern themselves with stacking.

However, there are cases where it does present problems. If you want to simulate actual nucleotides (see section 13.12), for example, then each base position must be unambiguously either A, T, G, or C; it makes no biological sense for an A and a G to be "stacked" at a single position. Similarly, if you want to make a quantitative-genetics model with particular discrete quantitative effects for the alleles at each QTL (see section 13.1), such as a −1/0/+1 allelic system, you would not want mutation stacking to occur since stacking of more than one mutation at a given QTL would violate your design. The default mutation stacking behavior may therefore be modified, and indeed, the two example recipes cited above do so.

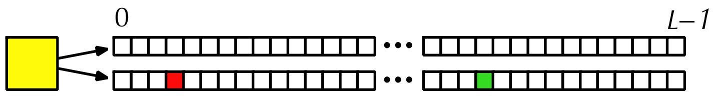
The stacking behavior of mutations is governed by their *mutation type*, a concept we haven't yet discussed. All mutations in SLiM belong to a mutation type, represented by the Eidos class `MutationType` (section 21.9). Mutation types are important primarily because they dictate the distribution of fitness effects from which mutations are drawn; all of the mutations of a given mutation type might be neutral, for example, or they might be deleterious and drawn from a gamma distribution, for example. When a new mutation is generated by SLiM, the selection coefficient for the mutation is drawn from the distribution specified by the relevant mutation type, as will be discussed in detail in section 1.5.4. Simulations may define as many mutation types as desired, but most simulations contain just one or a few mutation types.

Besides defining the distribution of fitness effects from which mutations are drawn, mutation types define a few other behaviors for mutations too. For example, the `convertToSubstitution` property mentioned in section 1.5.2, which determines whether a mutation will be removed when it fixes, is actually a property of `MutationType`, not of each individual mutation, since it makes sense for this behavior to be uniform across each class of mutations. The dominance coefficient of mutations is also a property of the mutation type, not individual mutations, for the same reason.

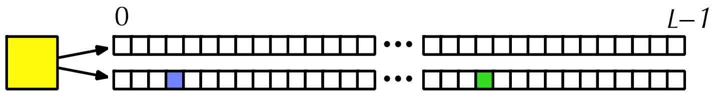
For our discussion of mutation stacking here, however, mutation types are important because stacking behavior is controlled by the `mutationStackGroup` and `mutationStackPolicy` properties of `MutationType` (see section 21.9.1); all of the mutations of a given mutation type follow the same stacking policy. In fact, more than one mutation type can be joined together into a single "mutation stacking group" using `mutationStackGroup`, and then all of the mutations in that stacking group follow the same policy. This is a power-user feature that we will mostly gloss over for the rest of the discussion here, however; we will just assume that each mutation type constitutes a separate stacking group (which is the default behavior).

Given this, in the example above the red mutation needs to be of the same mutation type (or in the same stacking group) as the blue mutation before stacking can be prevented. If they are not of the same mutation type (or more precisely, not in the same stacking group), then they will stack, regardless of what stacking policy has been set for each mutation type. The idea is that you generally don't want different kinds of mutations to interfere with each other in a model. If a QTL mutation exists at a given position, for example, then you might want a new QTL mutation at the same locus to replace the old one, rather than stacking – but if a neutral mutation occurred at the same locus, you would certainly not want that neutral mutation to replace the existing QTL mutation! Whatever you might think of that argument, you can always modify it by placing all of your mutation types into a single stacking group.

So let's now assume that the red and blue mutations are in the same stacking group – of the same mutation type, most trivially. Now the stacking policy can be modified. The default policy is referred to as type `"s"` (for "stack"), and yields the stacked result we saw above. Instead, you can set the policy to type `"l"` (for "last"), which produces this result after the red mutation occurs:

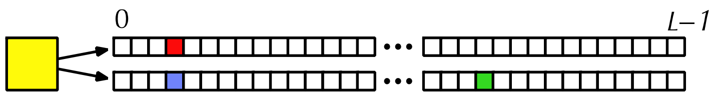


The red mutation has replaced the mutation in this genome, because this stacking policy dictates that the *last* mutation at a given position should be kept. This is the common alternative to the `"s"` policy, but you can also set a policy of `"f"` (for "first") which produces this result:

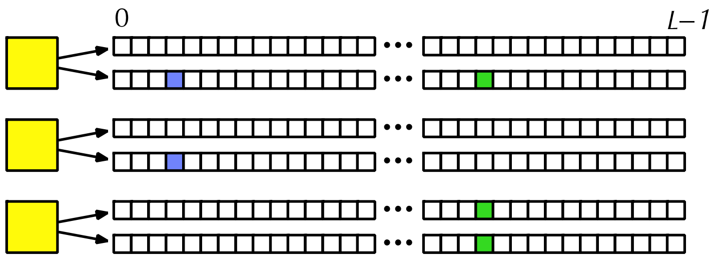


Here the red mutation has simply been thrown away, because the blue mutation was there first. The post-mutation state is therefore identical to the pre-mutation state (note that this means the effective mutation rate will be lower than the requested mutation rate, since some mutations will be suppressed). In general, this policy retains the *first* mutation at a given position in a given genome; new mutations are only allowed in if the position is presently empty. This is less commonly used, since its biological motivation is unclear, but it is provided as an option in SLiM just in case it is called for in some unusual situation.

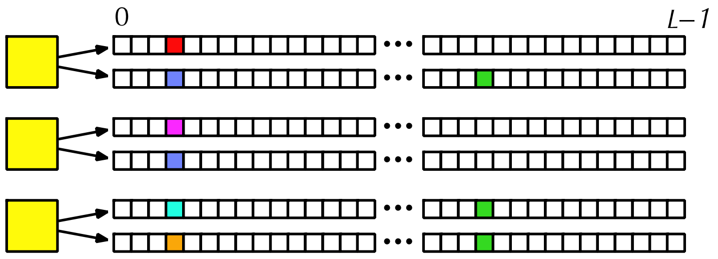
Note that all three stacking policies – `"s"`, `"l"`, and `"f"` – depend only upon the existing mutation(s) *at the specific base position in the specific genome* where a new mutation is occurring. The state at other positions, or in other genomes, is completely irrelevant. Changing the mutation stacking policy is not a way to prevent more than one allele from existing in a population at a given locus; it is only a way to prevent more than one mutation from existing *in one genome* at a given locus. Suppose, in our ongoing example, that the new red mutation had occurred in the *other* genome of the individual instead; regardless of the stacking policy, the result would then be:



That base position in that genome was empty; the stacking policy is therefore irrelevant, since there is no pre-existing mutation to stack on top of, so the red mutation is always added. More generally, suppose we have a population of three individuals, with a few mutations:



Different new mutations could occur at each of the empty sites at base position 3, regardless of the stacking policy. So whether the stacking policy is `"s"`, `"l"`, or `"f"`, new mutations could easily lead to this state:



If the stacking policy were `"f"`, further new mutations at position 3 beyond this could not be introduced; now that every genome has a mutation at position 3, those pre-existing mutations would prevent the new mutations from being added. Under stacking policy `"l"`, new mutations would still be possible at position 3 even in this state; the new mutations would just replace the old mutations. Under policy `"s"`, the new mutations would stack, the default behavior.

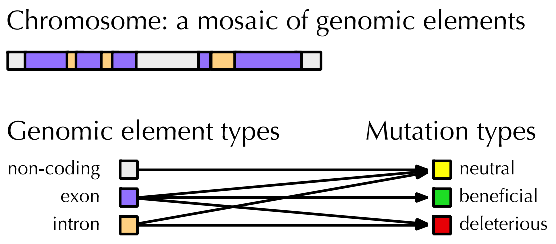
Sometimes it is desirable to allow for the possibility of back-mutation in a model. This can be accomplished in several ways in SLiM. One way is to use a mutational distribution of fitness effects that provides only a limited set of possible values (perhaps four values, to represent the four possible nucleotide at a base position), and use type `"l"` stacking so that new mutations replace existing mutations; new mutations are then automatically sometimes back-mutations. See section 13.12 for an example of this sort of strategy. Another possibility, if you only need back-mutation to the "wild type" empty-genome state, is to remove existing mutations yourself, in script; if done with the appropriate probability, this could simulate back-mutation to the wild type.

Finally, note that the stacking policy is applied to new mutations introduced in script, as well as to new mutations added by SLiM as a result of the overall mutation rate. New mutations that you add will be allowed to stack unless you change the stacking policy; and conversely, if you change the stacking policy then new mutations that you add might result in the removal of pre-existing mutations, or might not be added at all, in accordance with the policy you have chosen. However, when the stacking policy is changed in mid-run it is not retroactively enforced upon existing mutations, and when a saved population is loaded the current stacking policy is not enforced upon the individuals loaded.

The issue of mutation stacking is a bit complicated and confusing; if the discussion above has left you with more questions than answers, rest assured that this is an advanced topic that generally does not impact simple models at all. Play around with SLiM for a while, and then when you revisit this section it will probably make much more sense.

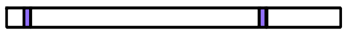
1.5.4 Genomic elements, genomic element types, mutation types, and the chromosome

SLiM allows you to model complex chromosomes with genomic regions that have different mutational effects. For example, exons would be expected to sustain beneficial, deleterious, and neutral mutations, whereas introns might sustain only deleterious and neutral mutations, and non-coding regions might only allow neutral mutations. You set up this structure in SLiM using a hierarchical configuration: the chromosome (class `Chromosome`, section 21.2) contains genomic elements (class `GenomicElement`, section 21.4), which are each of a given genomic element type (class `GenomicElementType`, section 21.5), and each genomic element type draws new mutations from a weighted set of mutation types (class `MutationType`, section 21.9), each of which specifies a distribution of fitness effects for that type of mutation. In an exon/intron/non-coding model, for example, each type of genomic region – "exon", "intron", and "non-coding" – would be a genomic element type, and the chromosome would be a mosaic of genomic elements using these three genomic element types. Each of these genomic element types would draw its mutations from a different set of mutation types – perhaps "beneficial", "deleterious", and "neutral", in this case. In practice, that might look something like this:



Here the chromosome contains two genes, each of which is composed of an alternation of exons and introns, and non-coding regions are interspersed around the genes. Those regions along the chromosome are defined by genomic elements, which reference the three genomic element types defined here (non-coding, exon, and intron). Those three genomic element types each utilize some subset of the mutation types that have been defined here (neutral, beneficial, and deleterious). Although this diagram simply shows arrows from genomic element types to mutation types, there are in fact weights associated with the mutation types of a given genomic element type; in this case, you might specify that 90% of mutations within introns are neutral and 10% are deleterious, by giving those weights to SLiM when the intron genomic element type is configured. In this way, new mutations that are automatically generated by SLiM will have appropriate fitness effects depending upon the genomic region in which they occur.

Note that this example is entirely arbitrary; you can define whatever mutation types, genomic element types, and genomic elements you wish. You could make your chromosome entirely neutral, or you could model the specific mutational effects of each region in an empirical genome map, right down to the full level of detail known for your study organism. There is no practical limit to the number of mutation types and genomic element types you may define. In the opposite direction, you can also make a much simpler model than the one above. Not all of the chromosome needs to be assigned to a genomic element; much of the chromosome can simply be empty. For example, you could make a model of epistatic interactions between two loci with a chromosome like this:



Here most of the chromosome is empty, containing no genomic elements. No mutations will be generated in these regions, since mutation generation in SLiM is governed by genomic elements. Only the purple loci will be active; we have one genomic element type and one mutation type in this model, and quite possibly only two mutations (one at each locus). A simple genetic structure like this will often run much faster in SLiM than simulating a whole chromosome; if you are not interested in what is going on in some regions of the chromosome, just don't simulate it. The only limitation in setting up your chromosome structure in SLiM is that genomic elements must be non-overlapping.

Note also that in general, this chromosomal structure only influences the way that SLiM generates new mutations. When offspring are generated, the overall mutation rate is used to draw the number of mutations that have occurred in a given gamete. The position of each mutation is then drawn, and SLiM determines which genomic element the mutation falls within. Given that, SLiM can find the genomic element type, and it then chooses a mutation type from the weighted set of mutation types used by that genomic element type. Finally, knowing the mutation type for the mutation, it draws a selection coefficient from the distribution of fitness effects for that mutation type. That yields a new mutation object, which is placed in the gamete. That is the only time that SLiM uses the genomic elements and genomic element types you have defined; none of the other machinery inside SLiM's core cares about those constructs at all. You may consult the chromosomal structure in your script and use it in whatever way you wish, but doing so would be quite unusual. By and large, the behavior of SLiM simulations depends upon the mutations contained by the genomes of individuals, without reference to the chromosomal structure after the point when new mutations are created.

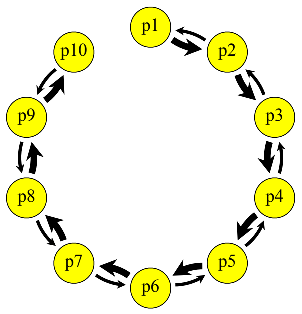
Mutation types, however, do continue to be used, in a minimal fashion, as we saw in section 1.5.3; each mutation knows its mutation type, and some properties of mutations, such as their dominance coefficient, their stacking behavior, and their fixation behavior, are specified by their mutation type.

1.5.5 Subpopulations and migration

The previous section discussed hierarchy levels from the individual to the genome to the mutation, and the dependence of mutations upon mutation types, genomic element types, genomic elements, and ultimately the chromosome itself. However, there are also higher hierarchy levels: individuals live within subpopulations, and all of the subpopulations together exist within the whole modeled population.

Subpopulations are represented by the class `Subpopulation` in Eidos. A subpopulation is a set of individuals, and is characterized primarily by the fact that random mating occurs (weighted by individual fitness) within each subpopulation. In other words, subpopulations primarily influence reproductive isolation; each subpopulation is internally panmictic (again, weighted by individual fitness), but externally isolated. Migration rates can be configured between subpopulations in order to allow gene flow, but by default the migration rate among subpopulations is zero.

For example, one might have a population structure like this:



Here we have ten subpopulations linked into a "stepping-stone" model that might represent a river system; subpopulation `p1` is upstream, and relatively high levels of migration produce gene flow in the downstream direction, while much lower levels of migration exist in the upstream direction (as shown by the relative widths of the arrows). This is just an example; you can have as many subpopulations as you wish, linked by any pattern of migration. The effect of the population structure on SLiM will manifest in the pattern of reproductive isolation among individuals.

The details of this conceptual model can be important. Offspring are always generated by parents within a single subpopulation; parentals do not migrate between subpopulations for the purposes of mating (in WF models, to which we are still limiting this discussion; see section 1.6). Instead, migration occurs at the juvenile stage in SLiM; generated offspring are placed into particular subpopulations in accordance with the specified migration rates. SLiM allows you to define spatial simulations involving one-, two-, or three-dimensional landscapes for each subpopulation; again, even in such spatial models, panmixis (weighted by individual fitness) is the default, although effects like spatial competition and spatial mate choice preference may be added in script. The subpopulation is the fundamental unit of reproductive isolation in SLiM.

An important conceptual point is that when setting the size of a subpopulation in SLiM, this should be thought of as a request for a future change, not as a present-time change. If a subpopulation contains 800 individuals and the script requests that it be 900 or 700 instead, that change does not happen immediately (which individuals would be removed? how exactly would the new individuals be created – with what genetic state?); instead, the subpopulation size change is a request that will take effect in the next generation. That is, when offspring are generated, 900 or 700 offspring will be generated from the current subpopulation of 800, and the requested subpopulation size will thus take effect in the child generation. This is always the case in SLiM; there is actually no straightforward way to create new individuals or kill existing individuals within a single generation (although the fitness of an individual can be set to zero, which has much the same effect as killing it, all else being equal).

Another key concept is that zero-size subpopulations do not exist in SLiM. If a subpopulation is set to size zero, it will (in the child generation) cease to exist entirely. For this reason, a new subpopulation cannot be created with a size of zero, since that has no meaning in SLiM. Instead, you should create the new subpopulation with a non-zero size at the moment that its size grows above zero. This can be inconvenient in metapopulation models that involve dynamic local extinction and re-colonization; such models are better written as nonWF models, which follow very different rules (see section 1.6, and section 15.5 for an example of a nonWF extinction/recolonization model).

1.5.6 Other concepts

That completes our overview of the foundational concepts underlying SLiM. There is a lot more to SLiM that will be covered in the following chapters, but if you understand these fundamental ideas the rest should be fairly straightforward.

Other sections of this manual also provide important conceptual information. Section 1.3 contains a brief introduction to some other key SLiM concepts that did not merit an in-depth discussion here, such as fitness, the life cycle, continuous space, interactions, and tags; it would be good to read now, if you haven't already. Part II of this manual, the SLiM Reference, also has some conceptual sections; chapter 19 contains detailed information on the stages of the generational life cycle in SLiM for WF models (and chapter 20, for nonWF models), including details on how mate choice, migration, offspring generation, fitness calculation, and other stages are implemented, and chapter 22 describes how to modify those default life cycle stages through the use of several different types of scripted callbacks, which provides much of the power and flexibility of SLiM. Reading those chapters might be deferred until you have become more familiar with SLiM, however, as they are more technical; if you are a beginning SLiM user, it is recommended that you finish reading this chapter and then proceed with installing SLiM and begin experimenting with the recipes presented in the chapters that follow.

1.6 Wright-Fisher (WF) versus non-Wright-Fisher (nonWF) models

SLiM 1.x and 2.x supported only one type of model, Wright-Fisher models (henceforth referred to as WF models). In SLiM 3.0, support has been added for a second type of model, non-Wright-Fisher models (henceforth, nonWF models). The choice between these types of models is made with an optional initialization call, `initializeSLiMModelType()`; if no call to that function is made, the WF model type is used by default, providing complete backward compatibility with SLiM 2.x.

Use of the nonWF model type is an advanced topic, recommended only for users experienced with SLiM. Most of this manual will be about the default WF model type. Only three areas of this manual will discuss nonWF models: section 1.6 (e.g., this section, which summarizes the differences between WF and nonWF models), chapter 15 (which introduces nonWF models in more detail, and then presents nonWF model recipes), and the SLiM Reference (Part II of this manual).

The differences between WF and nonWF models are pervasive, but may be regarded as falling into a few major categories:

- **Age structure.** In WF models, generations are discrete and non-overlapping. Each "tick" of SLiM's generation counter is associated with the creation of a new offspring generation and the demise of the previous parental generation. There is thus no concept of the age of an individual, since all individuals live for a single "tick". In nonWF models, generations may instead be overlapping. Each "tick" of SLiM's generation counter is associated with the opportunity for creation of new offspring and the opportunity for mortality among existing individuals. SLiM keeps track of the age of individuals, which may live for many "ticks". This makes it simple to construct models of overlapping generations with any type of age structure and any age-related behaviors desired.

- **Offspring generation.** In WF models, offspring are generated automatically by SLiM each generation. This process may be modified by various callbacks, but the process itself – how many offspring to generate, from which parental individuals, into which subpopulations – is managed by SLiM in such a way as to "fill out" each subpopulation with a fresh batch of offspring while satisfying the constraints imposed by parameters such as subpopulation size, sex ratio, cloning rate, and selfing rate. In nonWF models, offspring are instead generated in response to a request from the model script, made in a `reproduction()` callback, and the script itself is in charge of managing the process. In nonWF models, SLiM no longer attempts to enforce any particular subpopulation size, sex ratio, cloning rate, or selfing rate; typically, these are instead emergent properties of the individual-based dynamics of the model. This approach is somewhat more complex, but allows the genetics and state of each individual to influence the way that individual reproduces – its expected litter size, its reproductive behavior (cloning, selfing, biparental mating), the sex of its offspring, and so forth.

- **Population regulation**. In WF models, population regulation (keeping population size within bounds) is managed automatically by SLiM, which keeps each subpopulation at the initial size it is given, or at whatever new size is set by a `setSubpopulationSize()` call. Subpopulation size is therefore a parameter of the model, in effect. In nonWF models, population regulation is instead an emergent property, a side effect of how many offspring are created versus how many individuals die due to selection in each generation. This makes it much more natural to construct models with realistic population dynamics such as density-dependence, fitness-dependence, resource limitation (i.e., carrying capacity), and so forth. In a nonWF model, the parameters of the model that result in population regulation would more likely be things like carrying capacity, the strength of density-dependent selection, or the size of a limited resource pool.

- **Fitness.** In WF models, all offspring survive to maturity, and fitness specifies the probability that an individual will be chosen as a parent in the next generation. Higher-fitness individuals thus have a larger expected litter size, but fitness in WF models is *relative* fitness because the population size is held to whatever size is set by the model as described above. In nonWF models, fitness influences survival instead (mating success and fecundity can be modified also, but in script, not through SLiM's automatic fitness evaluation mechanism). Fitness differences are thus expressed through the likelihood that a given individual will survive to maturity. This allows a more realistic modeling of the variance in reproductive output, as well as simplifying model dynamics that are influenced by the survival of individuals, such as competition. In nonWF models, fitness is *absolute* fitness, which is more realistic but can be more challenging to model since it forces you to think explicitly about population regulation in concrete, individual-based, mechanistic terms.

- **Migration.** In WF models, migration is governed by model parameters set on each subpopulation, specifying what rate of migration SLiM should enforce with each other subpopulation. Migration is simulated in these models as the movement of an offspring individual, immediately after it is generated in the parental subpopulation; thus, only juvenile migration can be modeled. In nonWF models, migration is instead implemented in script, by explicitly moving individuals from subpopulation to subpopulation. This can be done at any time; migration of adults as well as juveniles can be modeled, or multiple migrations over the course of an individual's life. This design also makes it much simpler to implement migration that depends upon the circumstances of each individual: habitat choice, condition-dependent migration, genetic variation in dispersal, sex differences in migration behavior, and so forth.

- **Subpopulation splits.** In WF models, the splitting of a subpopulation is modeled as a new subpopulation being founded by a wave of such migrant offspring. In nonWF models, subpopulation splits are modeled as the migration of a set of individuals (of any age) to form a new subpopulation. Particularly in models with small population sizes, this can produce more realistic splits, particularly when migration of parental individuals, rather than juveniles, is desired to found new populations.

The general trend across all of the above points is that nonWF models are more individual-based, more script-controlled, and potentially more biologically realistic – but also more complex in some respects, because the SLiM core is managing fewer details of the model's dynamics automatically. In particular, all nonWF models must implement at least one `reproduction()` callback in order to generate new offspring. Each type of model has its appropriate uses; nonWF models are not "better", although they are more flexible in some respects. WF models may be simpler to design, and may run considerably faster; and of course staying within the WF conceptual framework may make it easier to compare simulation results with theoretical expectations from analytical models that are based in the Wright-Fisher paradigm.

As mentioned above, most of the remainder of this manual will discuss WF models, since they are SLiM's original mode of operation and remain the default model type. Whenever a given section does not explicitly state otherwise, it should be assumed that the focus in on WF models. All of the recipes in Part I of the manual are WF recipes up until chapter 15, which specifically presents nonWF models.

The reference section of this manual, Part II, will provide reference information covering both WF and nonWF models. A color-coding convention will thus be used in Part II: items which apply only to WF models will be highlighted in green, and items which apply only to nonWF models (or primarily so) will be highlighted in blue. For example:

```
– (void)a_WF_only_method(...)
```

and:

```
– (void)a_nonWF_only_method(...)
```

Again: nonWF models are an advanced topic. As a beginning SLiM user, it's good to know that nonWF models exist, but don't worry if all of the above information is not clear. You can forget about nonWF models for now, and focus on familiarizing yourself with the default, WF models.

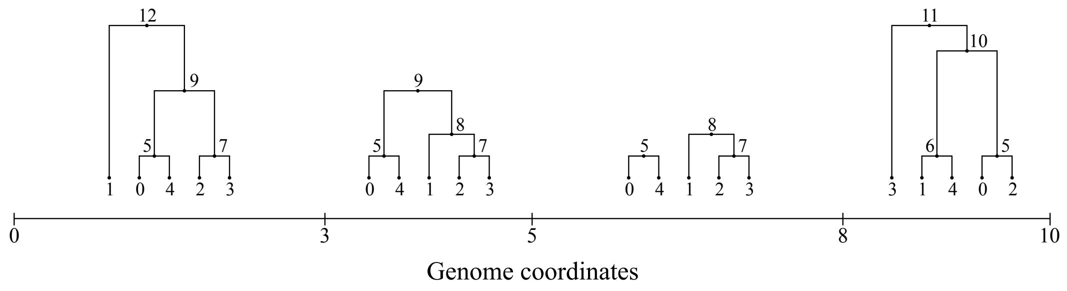
1.7 Tree-sequence recording

SLiM 3 introduces a major feature called tree-sequence recording. This is essentially a method of tracking the true local ancestry of every chromosome position in every individual as a SLiM model runs. Such ancestry information can be saved out to files called `.trees` files, and can be loaded in to SLiM from `.trees` files as long as they are in the correct SLiM-compliant format. These `.trees` files can also be loaded into Python, where their ancestry information can be browsed, analyzed, and even modified using the `msprime` coalescent simulation package. When moving data between SLiM and `msprime`, the `pyslim` Python package is also essential, since it knows how to translate some types of SLiM-specific information in `.trees` files from SLiM into a form that `msprime` can work with, and vice versa. Models that use tree-sequence recording will sometimes be referred to as *tree-seq models* for brevity.

Use of tree-sequence recording is an advanced topic, recommended only for users experienced with SLiM. Most of this manual will be about models that do not use tree-sequence recording. Only three areas of this manual will discuss tree-seq models: section 1.7 (e.g., this section, which summarizes the concept of tree-sequence recording), chapter 16 (which presents tree-seq model recipes), and the SLiM Reference (Part II of this manual).

Tree-sequence recording does not record the full pedigree of a model. Instead, it records only the specific ancestral information needed to reconstruct the mutational and recombinational history of each extant individual's genomes. Over time, some information that originally needed to be recorded in the tree sequence may become unnecessary to keep; perhaps a whole branch of the evolutionary tree went extinct and so the information recorded about it is no longer relevant, for example. Through the process of *simplification*, which is performed periodically upon the recorded tree sequence, all information that is not relevant to any extant genomes gets pruned away, which keeps the memory requirements of tree-sequence recording manageable.

This recorded information is referred to as a "tree sequence" because it is literally a sequence of trees. Conceptually, each position along the chromosome has its own ancestry tree, which is the result of recombination at that position; as one walks along the chromosome, one encounters a sequence of such ancestry trees, from which the pattern of inheritance can be traced from every extant genome back to the most recent common ancestor for the population at that chromosome position. The ancestry tree at a given position may have multiple roots, if there is no common ancestor for all of the individuals in the population at that position; forward simulations begin with every individual unrelated to every other, and common ancestry is only built over time through the process of coalescence. The ancestry trees at adjacent chromosome positions are generally highly correlated, and indeed are often identical (since those adjacent positions may never have been split by recombination, or traces of such recombination might not have survived in any living individual). Tree-sequence recording accounts for this correlation, tracking each distinct ancestry tree along successive chromosome intervals rather than at every position. This is one reason why the tree sequence is sometimes called a *succinct tree sequence*; it is much more compact than the full set of trees for every position, because it omits the redundant information shared between positions with identical ancestry. This multiplicity of trees is not easy to depict, but here is a sketch of the concept:



The intervals between the ticks on the *x* axis are intervals on the chromosome that have distinct ancestry trees (this example chromosome is only ten base positions long, and has four intervals with distinct trees). Each interval's ancestry tree reflects its particular pattern of inheritance along the chromosome; however, the trees at adjacent sites tend to be highly correlated, with redundant information that is represented concisely by the tree sequence data structure. Within each tree, the leaf nodes at the bottom (labeled 0 through 4) might be extant genomes with no descendants, whereas the internal nodes might be ancestral genomes that are no longer extant; however, with overlapping generations things might be less clear-cut, since ancestors might still be extant. As mentioned above, the tree for a given interval might have multiple roots, if coalescence is not yet complete; that situation is found in the ancestry tree for the third chromosome interval pictured above.

This is just a brief summary of tree-sequence recording, and may or may not be comprehensible; for a full overview of tree-sequence recording, including details of how simplification works, please refer to the definitive paper on the topic, Kelleher et al. (2018).

Tree-sequence recording enables some very powerful techniques, such as:

- **Overlaying neutral mutations.** You can run a model without any neutral mutations (which is generally much faster), and then overlay neutral mutations afterwards. This gains tremendous efficiency from the fact that neutral mutations only need to be overlaid on branches of the ancestry tree that lead to extant individuals; neutral mutations on all branches that went extinct before the end of the simulation do not need to be considered at all. For models that contain many neutral mutations, this can result in a speedup of an order of magnitude or more.

- **Analyzing ancestry directly.** You can sometimes avoid simulating neutral mutations altogether, when it is actually the pattern of ancestry you are interested in. Often the pattern of neutral mutations from a forward simulation is used to infer things about a population's history – selection, bottlenecks, immigration, and so forth. Using neutral mutations for this purpose is a blunt instrument, however, since they are sparse and occur stochastically; inference from them is difficult, time-consuming, and inexact. Instead, it is often possible to draw such inferences from the recorded tree sequence itself, which in a sense embodies every possible mutational history that the population could have had given its actual history of inheritance and recombination. The inferential power can therefore be much higher. This means that inferences from the tree sequence can often be exact, and can also often be computed much more quickly and easily than from neutral mutations.

- **Detecting coalescence during forward simulation.** Often you want to "burn in" a model until it has reached an equilibrium state, which can often be defined as occurring when full coalescence across the whole chromosome has occurred. The time at which this happens, however, is often hard to know. A heuristic of "10*N*" (running for a number of generations equal to ten times the population size) is often used, but even for simple models it can be an underestimate. For models with a variable population size, multiple subpopulations, or non-neutral dynamics of any kind, the proper burn-in duration is often just a guess, and it is often necessary to make a large overestimation "just to be safe". With tree-sequence recording enabled, SLiM can tell you whether your model has coalesced fully or not; it has all the information needed. You can then use that information to decide when to end the burn-in period of the model.

- **Moving between coalescent and forward simulation methods.** Tree-sequence recording and the `.trees` file format build a sort of bridge between coalescent and forward simulation methods, allowing both methods to be used in a single simulation. For example, a neutral "burn-in" period for a model could be simulated using the coalescent, and the results saved to a `.trees` file in the proper SLiM-compatible format using `pyslim`. That `.trees` file could then be loaded into SLiM as the starting state for forward simulation; perhaps the neutral mutations from the coalescent become non-neutral at that point in time, for example, due to a change in the environment, and so now one wishes to simulate the resulting non-neutral dynamics. Since the coalescent is so fast, this can result in much quicker burn-in compared to simulating the burn-in with SLiM. Overlaying neutral mutations after a run, mentioned above, is another strategy that moves between coalescent and forward simulation methods. Moving between methods in this manner allows the strengths of each method to be leveraged, while avoiding their weaknesses. As mentioned above, the `pyslim` package is essential to this sort of interoperability, as we will see in chapter 16. The `pyslim` package is not yet able to annotate mutations that were overlaid with `msprime` in a way that renders them SLiM-compatible, unfortunately; this planned feature is still being implemented. Several other ways of moving `.trees` data between SLiM and `msprime` using `pyslim` have been implemented, and will be shown in chapter 16.

- **"Recapitating" to construct the ancestral history of a simulation.** With this technique, you could run a model forward with no neutral burn-in period at all, from a set of empty genomes, and then reconstruct the ancestry of the initial genomes using the coalescent after the forward simulation has completed. This technique, called *recapitation*, is much more efficient even than generating a burned-in state using the coalescent directly, because only the ancestry trees present at the end of forward simulation need to be coalesced back; any part of any genome that was present in the initial state of the model but was later lost does not need to be coalesced, so most of the work of burn-in can be avoided. As before, neutral mutations can be overlaid at the end of the model run, after recapitation has constructed the ancestral history, rather than having to be simulated. This technique can allow very large models to be simulated relatively efficiently, since most of the work of burn-in can be eliminated. Support for this technique is presently being added to the `msprime` Python package; this feature will be rolled out in a later release of SLiM.

Tree-sequence recording has a large impact on the performance of models, in terms of both runtime and memory usage. It is therefore disabled by default, and needs to be enabled with a call to an initialization function, `initializeTreeSeq()`. When it is enabled, you can control the frequency of simplification (more frequent simplification means a lower memory footprint but a longer runtime), and you can turn on checking for coalescence if your model needs to know when full coalescence has been attained (for a small additional performance penalty on top of each simplification).

Again, tree-seq models are an advanced topic; it is good to know that tree-sequence recording is an option, but beginning SLiM users should postpone trying to use it until they have become fairly familiar with the basics of SLiM. However, if you're finding that performance is an issue, and you're bogged down simulating huge numbers of neutral mutations or running endless burn-in periods, tree-sequence recording may be able to help. Similarly, if you want to detect coalescence, or obtain a record of the ancestry at every chromosome position, tree-sequence recording can provide a solution. Tree-sequence recording also provides an output format for saving simulation state that can be much more compact than either VCF or SLiM's native output file format (even though it includes information about ancestry that those file formats do not), and that can be analyzed and manipulated in Python with `pyslim`; these advantages can also be a reason to use tree-sequence recording.

1.8 Online resources for SLiM users

Users of SLiM should be aware of various online resources that are available to support their work. This section summarizes them and provides links.

- First of all, there is the **SLiM home page** at the Messer lab website. This is the primary place from which to download SLiM, and provides a history of SLiM releases as well as a list of publications that have used SLiM. https://messerlab.org/slim/

- The **slim-announce mailing list** is only for announcements from our group, such as new versions of SLiM, new SLiM publications related to SLiM, and plans for conferences where you could connect with us. https://groups.google.com/forum/#!forum/slim-announce

- The **slim-discuss mailing list** is for questions from SLiM users that might be of general interest. Please feel free to post your own questions – and even to answer other people's questions, if you can. https://groups.google.com/forum/#!forum/slim-discuss

- The **SLiM-Extras GitHub repository** is a place for the SLiM community to share useful resources related to SLiM. This could include reuseable Eidos functions (see, e.g., section

11.1), full SLiM models that might be of general interest, code for reading or analyzing SLiM output in languages like R or Python, code for sublaunching multiple SLiM runs on computing clusters (see section 1.4), and so forth. Please feel free to email us your own submissions for additions to SLiM-Extras. https://github.com/MesserLab/SLiM-Extras

- The **SLiM GitHub repository** is where SLiM's source code lives. SLiM is open-source, but unless you have some specific reason to want to access the source, you probably don't need to. As described in chapter 2, users on Mac OS X can install SLiM with the double-click installer we provide, and users on Linux will usually want to build from the official release source archive provided on the SLiM home page. The GitHub repository, then, is mostly useful for people who want to be on the cutting edge, running the latest version of SLiM before it has been publicly released. Be aware doing this will mean you are more exposed to bugs, and that sometimes the sources on GitHub may not even build (although we try to avoid that). https://github.com/MesserLab/SLiM

That's what we've got for now. As always, please contact us if you have suggestions for additions that would be useful, or reports of problems with any of the above.

2. Installation

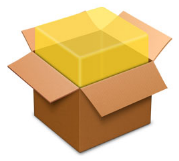
The command-line tool for SLiM is designed to be portable; it is written in pure C++, with no external dependencies. Code from various third-party libraries such the GNU Scientific Library (Galassi et al. 2009), Boost (Boost 2015), and msprime (Kelleher et al. 2016) is used in SLiM (see chapter 27), but that code has been integrated directly into SLiM, so those libraries are not required to build or run SLiM. SLiM should be buildable on Mac OS X, Linux, other Un*x platforms, and – possibly with minor modifications – on other platforms as well. The SLiMgui application, on the other hand, is written for Mac OS X only, in Objective-C++ using Apple's Cocoa library, and is available only on that platform. The steps to install SLiM depend upon the platform you are on; please refer to the appropriate subsection below.

2.1 Installation on Mac OS X

On Mac OS X you have a choice between (1) installing a prebuilt package containing the `slim` command-line tool and the SLiMgui application (as well as EidosScribe, the `eidos` command-line tool, and manual PDFs), or (2) cloning the SLiM GitHub repository and building the projects yourself using Apple's Xcode development environment. Unless you are an experienced developer, the first option is recommended. Building SLiM on OS X at the command line is *not* recommended, although it is possible; use of the Xcode project will provide the proper compiler settings, etc., for a standard OS X build.

2.1.1 Installing the prebuilt SLiM package on Mac OS X

This is quite straightforward. First, download the installer package from SLiM's home page at http://messerlab.org/slim/:



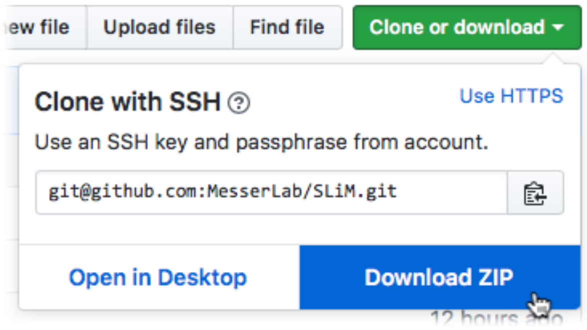
If multiple versions are available, be sure to download the appropriate version for your system. Once it is downloaded, double-click the package in the Finder to run the installer. Click through all steps in the installer, and SLiM will now be installed on your system. The applications (SLiMgui and EidosScribe) will be installed in your `/Applications` folder; the command-line tools (`slim` and `eidos`) will be installed in `/usr/local/bin/`. Pre-existing Terminal windows may not find `slim` and `eidos`; open a new Terminal window to get the updated paths.

2.1.2 Building SLiM from sources on Mac OS X

This option is relatively complex. If you are not an experienced developer it is recommended that you install SLiM using the prebuilt package instead (see the previous section). There is no advantage to building SLiM from sources unless you wish to run it under the debugger, modify its code, or other similarly advanced tasks, or wish to run the current development version of SLiM.

First of all, you need to have Xcode and Apple's other developer tools installed on your machine. SLiM's project is generally kept synchronized with the current version of Xcode; older versions of Xcode may be unable to open the SLiM project. To run the current version of Xcode, you generally need to be on the current version of OS X as well, so you may need to upgrade your OS X installation before installing Xcode. Once you have done that, you will need to obtain and install Xcode itself. This will probably involve registering as a developer with Apple (which is free, for the basic level) at their developer website, developer.apple.com, and then downloading and installing the developer tools package including the latest version of Xcode (which may be possible through the App Store, otherwise through the developer website's Member Center). It is quite a large download, so do it through a fast connection. Once you have completed this step, you should see Xcode.app in your `/Applications` folder, and you should be able to launch it by double-clicking it.

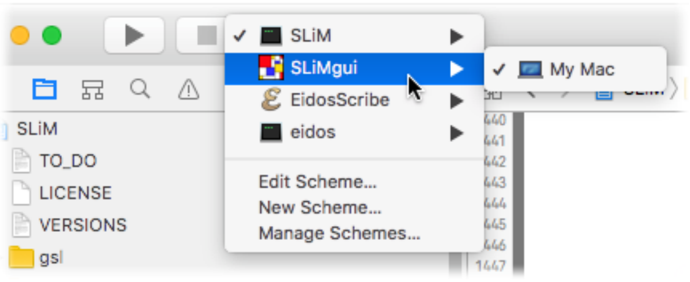
Second, you need to obtain the SLiM source code. If you are following these instructions, you probably want to obtain the current development version of SLiM from its GitHub repository at https://github.com/MesserLab/SLiM. Go to that URL, click the big green "Clone or download" button, and then click "Download ZIP":



Locate the downloaded file and double-click it to decompress the zip file if that has not already been done for you automatically by your browser. This distribution will include the sources to allow you build both the `slim` command-line tool and the SLiMgui interactive graphical modeling environment. Be aware that the current development version on GitHub may not be thoroughly tested – indeed, it may not even compile.

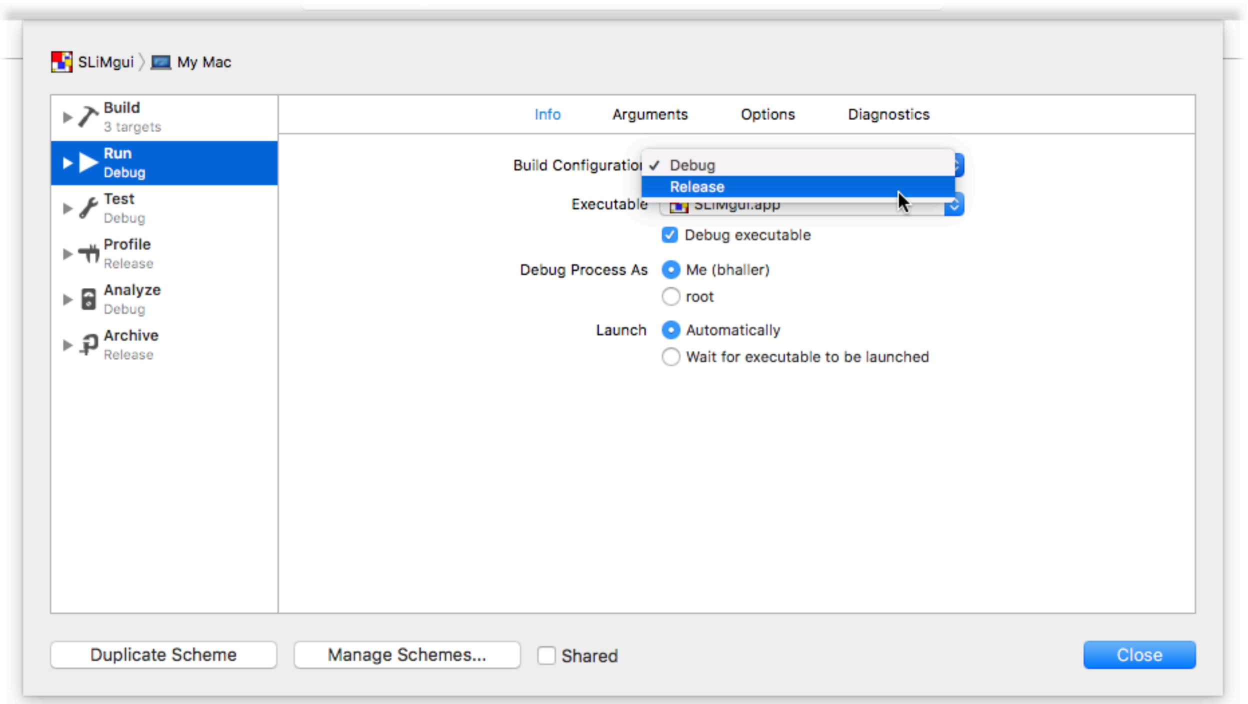
Third, open the SLiM project in Xcode. To do so, locate the Xcode project file within the archive you have just downloaded; it is at the root level, with the name `SLiM.xcodeproj`. Double-click it to open the project in Xcode. You should see a big project window.

Fourth, choose a build target. A target is basically a product that an Xcode project knows how to build. The SLiM project has four targets that may be selected: SLiM (the `slim` command-line tool), SLiMgui, EidosScribe (an interactive Eidos script development environment), and eidos (the Eidos interpreter command-line tool, `eidos`). For now, select SLiMgui. You do this in the pop-up near the upper left of the project window:



Fifth, build and run the selected target by pressing command-R (which is the Run command in the Product menu). It should build fairly cleanly (perhaps apart from some nib warnings that are difficult to eliminate). Once it finishes building (which may take several minutes, depending on your machine), SLiMgui should launch automatically. Assuming that worked, quit SLiMgui for now, as we are not quite done setting things up in Xcode.

Sixth, there is an additional twist: the build configuration and other build scheme options. These options are accessed by choosing the "Edit Scheme..." menu item that can be seen in the pop-up menu in the above screenshot. Choose this, and you will see a sheet:



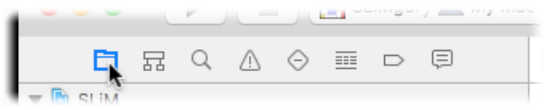
Build Configuration: ✓ Debug / Release
Executable: SLiMgui.app
[✓] Debug executable
Debug Process As: [● Me (bhaller)] root
Launch: [● Automatically] Wait for executable to be launched

In this screenshot, the "Run" action has been selected on the left, so we are configuring what Running this target (the SLiMgui target) will do. At the top, the Info tab is selected, which provides the most basic configuration options. Finally, the pop-up menu next to the label "Build Configuration" has been clicked in order to choose the Release build configuration. In general, you will want to build and run SLiM and SLiMgui using the Release build configuration unless you have a specific reason to wish to do otherwise; Release builds are much faster than Debug builds, partly because of optimization, and partly because additional runtime checks are turned on in SLiM's code when building in the Debug configuration. After choosing Release, you can click the Close button, and command-R (run) will now build and run a Release build of SLiMgui.

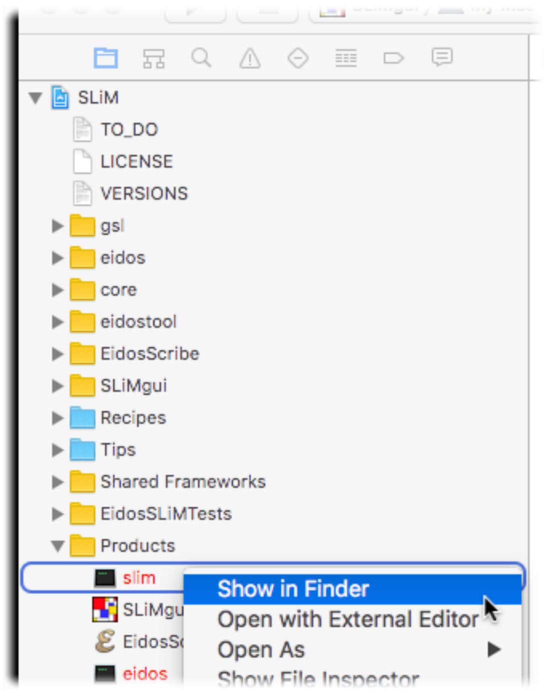
If your goal is to run SLiMgui, you can simply run it from within Xcode; there is no particular disadvantage to doing so. If your goal is to run the `slim` command-line tool, doing so from within Xcode is a little bit inconvenient (since it is a little bit complicated to supply command-line arguments to it, for example), so the simplest course is to build `slim` in Xcode and put the built executable wherever you want it to be so that you can run it in Terminal as usual.

To do this, first select the SLiM target from the target pop-up in the project window, as described above (since the SLiMgui target is presently selected, if you have been following along). Second, choose Edit Scheme... again and make sure that the SLiM target is using the Release build configuration for its Run action, as described above (since we set that for the SLiMgui target above, not for the SLiM target – each target has its own settings), and close the Edit Scheme... sheet. Third, press command-B to build the target (this is the Build command in the Product menu).

Once the build completes, you will want to locate the built product in the Finder. To do this, first select the Project Navigator in the project window by clicking the folder icon at the left edge of the strip of icons at the top left of the project window:



Then click disclosure triangles to open the SLiM top-level item and the Products subfolder in the outline view shown there:



The `slim` product may be shown in red even if it has been successfully built; this appears to be a bug in Xcode. Right-click (i.e., click with the right-hand mouse button) or control-click (i.e., hold down the control key and click) on the `slim` product, and choose “Show in Finder” from the context menu displayed, as shown in the screenshot above. Your computer should switch to the Finder and open a new window in the Finder, showing the contents of a folder that is probably named “Release” (because the Release build configuration has been chosen). A file named `slim` should be selected in this window. This is the built executable for the `slim` command-line tool. (There are other, more standard ways to get to this point, but they are a bit more complicated.) You should copy this file to whatever location you wish, and then run `slim` using that copy. The standard install location for slim is at `/usr/local/bin/`, but since this is a custom build it might be wise not to put it at that location to avoid confusion. Instead, a location like `~/bin/` inside your home directory might be appropriate (you might need to create this folder first, in the Finder). In any case, once you have installed `slim` at the desired location, you can open a Terminal window and `cd` to that location (your Terminal shell prompts may look different from mine, of course):

```
darwin:~ bhaller $ cd ~/bin
darwin:~/bin bhaller $
```

Then you can run the local copy of `slim` that is at that location:

```
./slim <rest of command line>
```

The syntax `./slim` tells Terminal to run the copy of SLiM in the current directory, rather than running the standard version that might be installed at `/usr/local/bin/` on your machine. You can verify that the correct version of SLiM is being run using the `-v` (version) option:

```
darwin:~/bin bhaller $ ./slim -v
SLiM version 2.3, built Apr 18 2017 17:20:34
```

The build date and time should correspond with the build you just did in Xcode; if not, you have done something wrong and should re-check the steps above.

You can in fact follow the same steps to locate the built SLiMgui application in the Finder and install it somewhere on your machine for later use; the `~/Applications/` folder might be a good choice of location. However, it is probably simpler to run it from within Xcode.

Obviously Xcode is a very complicated application, and we can't possibly provide a thorough introduction to using it, but the steps above should allow you to build and run both `slim` and SLiMgui using the current development head sources from GitHub. If you run into any problems with these instructions, please let us know.

2.2 Installation on Linux and other Un*x platforms

Details of building SLiM may vary depending on the platform, but the basic gist should be the same. First, you need to obtain the SLiM source code. It is recommended that you obtain the code for the latest supported release, from SLiM's home page at http://messerlab.org/slim/:

However, you may also obtain the current development version from SLiM's GitHub repository at https://github.com/MesserLab/SLiM. Be aware that the version on GitHub may not be thoroughly tested – indeed, it may not even compile.

The following steps have changed considerably with the release of SLiM 3, since we have switched from using the `make` build tool to using a tool called `cmake` that is considerably more modern (but also a bit more complicated to use). The `cmake` tool is often preinstalled on Linux systems, but if it is not installed on your machine, you will need to install it before proceeding. You can tell whether `cmake` is installed on your system by executing this in a terminal window:

```
which cmake
```

If a path is printed in response, `cmake` is installed; if not, it needs to be installed. On Mac OS X, `cmake` can be installed using MacPorts (https://www.macports.org) or Homebrew (https://brew.sh); which installation system you use seems to be largely a matter of taste, although you can read strong opinions in both directions online. On Linux and other Un*x systems, the `cmake` home page at https://cmake.org/download/ provides downloadable source packages with installation instructions. Apologies for this additional complication; with the integration of more third-party code into SLiM, using `make` directly just became too unwieldy. The `cmake` tool builds a makefile for us, which can then be used to build with `make`, as we will see next.

With `cmake` installed, go to a new Un*x shell window and type:

```
cd SLiM
cd ..
mkdir build
cd build
cmake ../SLiM
make slim
```

The first `cd` command changes the current directory to your SLiM source directory (you will need to supply the appropriate path there instead of just `SLiM`), and the next `cd` command changes to the enclosing directory (of course you can just `cd` there directly). We then use `mkdir` to create a build directory adjacent to the SLiM source directory in the filesystem; this keeps all of the cruft associated with the build process separate from SLiM's sources. We `cd` into that build directory, and then tell `cmake` to update its information regarding SLiM. The last command actually builds the `slim` command-line tool. Note that SLiM uses C++11 extensions; the g++ compiler installed on your machine must be recent enough to support C++11 or your build will fail. The `slim` tool will appear as an executable file in the `build` directory once the build is finished (not, as in SLiM 2.x, in a `bin` directory inside the source directory). You can copy the built executable to a different location, such as `/usr/bin/`, if you wish; the standard location for user-built executables depends upon your Un*x flavor, so consult your documentation if you wish to install it in a standard location.

The `eidos` command-line tool can also be built on Un*x platforms following the same procedure, with the final command `make eidos`; a simple `make` command will build both. The SLiMgui and EidosScribe targets are buildable only on Mac OS X using Xcode (see section 2.1.2).

Once `cmake`'s information has been set up, rebuilding after minor source changes can generally be done just by re-executing the `make slim` command in the build directory. If you make major changes to the SLiM sources – and in particular, if you add or remove source files, or do a `git pull` of new changes from GitHub – you might need to tell `cmake` to update its information before you run `make` to rebuild the project. This is necessary because SLiM's `CMakeLists.txt` configuration file uses a `cmake` feature called `GLOB` to collect a list of source files to be used for building, and that means that `cmake` cannot automatically re-update in all cases. If you make such changes to the sources, you should do the following:

```
cd SLiM
touch ./CMakeLists.txt
```

Then `cd` to the build directory and execute `make slim` to rebuild; `cmake`'s cached information will be rebuilt, since the configuration file was touched, so you do not need to re-run `cmake`.

The build instructions above use a build directory named `build`, and use a default "build type" with `cmake` (a Release build), and this will suffice for almost all SLiM users; you need not read further unless you really want to complicate your life. In fact, however, you can name your build directory whatever you wish, and you can have more than one build directory if you wish; and you can specify a build type of either Release or Debug with `cmake`. For example, you could do something like this to make a build directory named `Release`, using the Release build type:

```
cd SLiM
cd ..
mkdir Release
cd Release
cmake -D CMAKE_BUILD_TYPE=Release ../SLiM
make slim
```

A Release build has optimization turned on and debugging symbols turned off, giving you a lean, fast executable suitable for most purposes. This is `cmake`'s default when building SLiM; the original build instructions above produced a Release build since no build type was specified. Similarly, you could make a Debug build in a directory named `Debug`:

```
cd SLiM
cd ..
mkdir Debug
cd Debug
cmake -D CMAKE_BUILD_TYPE=Debug ../SLiM
make slim
```

A Debug build has optimization turned off and debugging symbols turned on, giving a large symbolicated build suitable for runtime debugging. Debug builds also have some additional runtime error checking turned on in SLiM, designed to catch a variety of internal error states that might cause a Release build to crash or produce incorrect output. Most users, however, will be fine with just the standard build directory named `build` and the default `cmake` build type.

2.3 Installation on non-Un*x platforms

Building and installing SLiM on non-Un*x platforms should be reasonably straightforward since the code is standard C and C++. However, there may be minor differences that lead to compile and/or link problems, particularly on non-POSIX-compliant operating systems such as Windows. We will probably not be able to give you any useful help in solving these problems; we know nothing about programming on Windows, for example. If you work through such problems and have useful patches for us to allow the project to build on a new platform (using `#ifdef` or similar for conditional compilation), feel free to send us a pull request on GitHub.

Overall, the build steps should be similar to the sections above: you will download the sources or clone the GitHub repository (see above), and then you will execute compile commands with (1) a flag indicating the C++11 standard, which is required for SLiM, (2) a nice high optimization level such as `-O3`, (3) all of the source files necessary, and (4) the appropriate header search paths. You can look at the project's `CMakeLists.txt` file for further guidance.

2.4 Testing the SLiM installation

Regardless of your platform or method of installation, it is a good idea to run some self-tests after installing SLiM. In your Terminal window, Un*x shell window, or platform equivalent, run the following two commands (while in the build directory where the `slim` executable resides):

```
./slim -testEidos
./slim -testSLiM
```

Each command should print a result line beginning with `SUCCESS` and then a count of successful self-tests. If any other lines print, indicating failure of a test, you should probably contact us to ask how to proceed.

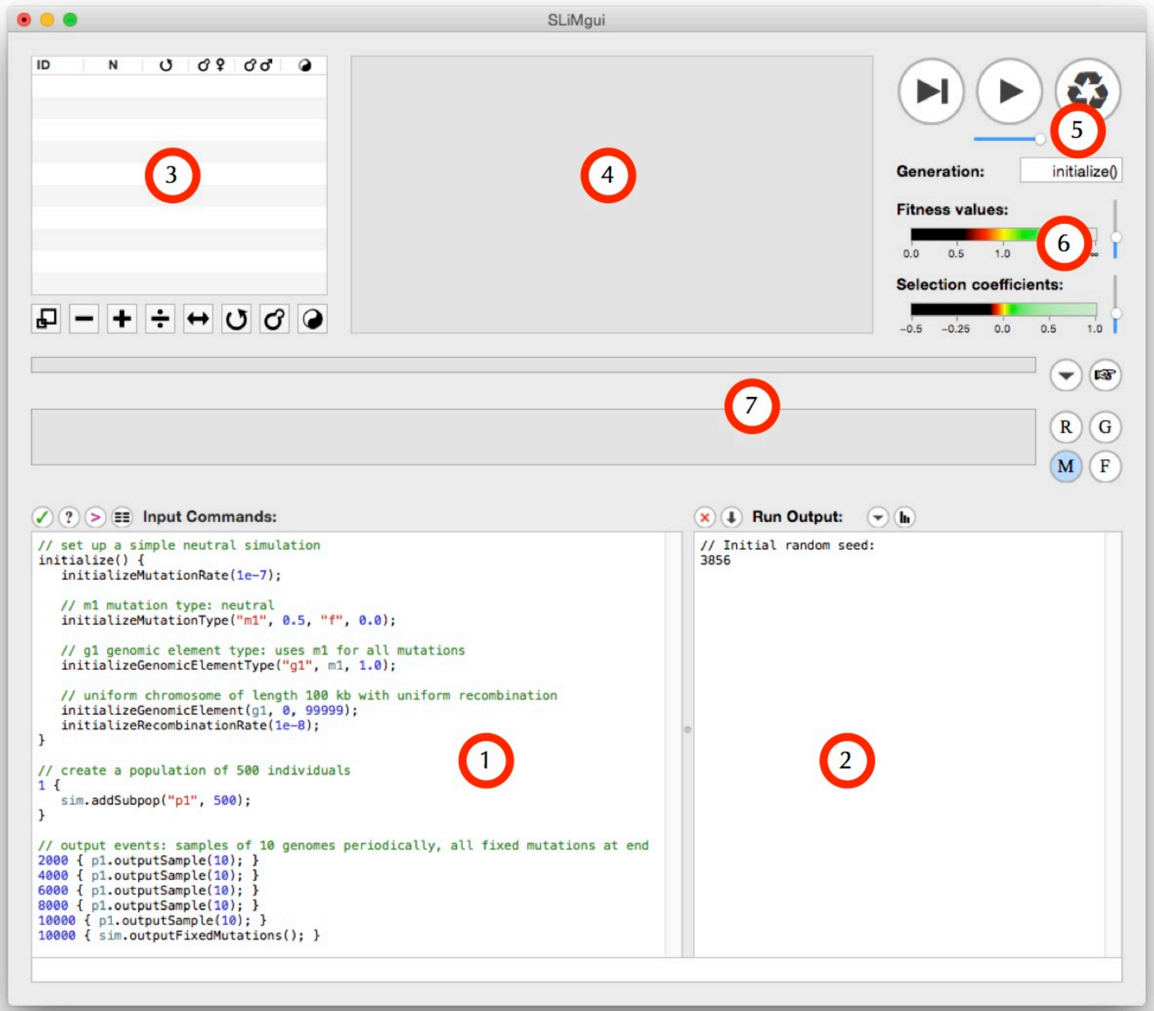
3 Running simulations in SLiMgui

This chapter introduces the SLiMgui graphical development environment for SLiM. This app is available only on Mac OS X; on other platforms you will need to run SLiM directly from the command line, in which case you can skip ahead to chapter 4.

On OS X, SLiMgui is typically located in `/Applications/` if you installed from the prebuilt package; if you built SLiM from sources, you may run SLiMgui directly from Xcode.

3.1 The SLiMgui simulation window

When you first launch SLiMgui, you should see a window similar to this:



```
// set up a simple neutral simulation
initialize() {
   initializeMutationRate(1e-7);

   // m1 mutation type: neutral
   initializeMutationType("m1", 0.5, "f", 0.0);

   // g1 genomic element type: uses m1 for all mutations
   initializeGenomicElementType("g1", m1, 1.0);

   // uniform chromosome of length 100 kb with uniform recombination
   initializeGenomicElement(g1, 0, 99999);
   initializeRecombinationRate(1e-8);
}

// create a population of 500 individuals
1 {
   sim.addSubpop("p1", 500);
}

// output events: samples of 10 genomes periodically, all fixed mutations at end
2000 { p1.outputSample(10); }
4000 { p1.outputSample(10); }
6000 { p1.outputSample(10); }
8000 { p1.outputSample(10); }
10000 { p1.outputSample(10); }
10000 { sim.outputFixedMutations(); }
```

```
// Initial random seed:
3856
```

The main sections of the window are indicated with red numbered circles; they are:

1. The scripting pane. This is where input commands for SLiM – in the form of an Eidos script – are entered. A simple script is given by SLiMgui by default, as a starting point. At the top of this pane you can see the pane's title, "Input Commands", and to the left of that title are buttons for four commands: Check Script, Script Help, Show Eidos Console, and Show Eidos Variable Browser

(all of the buttons in the window have tooltips, so you can just hover the mouse over them to be reminded of what they do). The use of these buttons will become clear in later sections.

2. The output pane. This is where run output from SLiM – diagnostic output as well as output explicitly generated by your simulation script – is shown. At the top of this pane you can see the pane's title, "Run Output", surrounded by buttons for four commands: Clear Output, Dump Population State, Add Output Command (a pop-up menu button), and Show Graph (also a pop-up menu button). Again, these buttons will be covered in later sections.

3. The population view. This is a table view that displays all of the subpopulations in the current simulation population. Since the simulation has not yet been started, there are presently no subpopulations, and thus the table is empty. This will be covered in more detail once we have a running simulation. Directly below the table view are eight buttons: Change Subpopulation Size, Remove Subpopulation, Add Subpopulation, Split Subpopulation, Change Migration Rates, Change Selfing Rate, Change Cloning Rate, and Change Sex Ratio. Again, these buttons will be covered in later sections.

4. The individual view. This is where individual "organisms" in the simulation are displayed from the subpopulation(s) selected in the population view. At present this is empty since there are no individuals to display.

5. The generation controls. The three large buttons are, from left to right, for the commands Step (to run forward one generation), Play (to run forward continuously), and Recycle (to reset back to the initialization stage of the simulation). The slider below the Play button controls the speed at which the simulation runs; usually you will want this to be the maximum speed, but occasionally it is useful to slow the simulation down to better see what is happening on short timescales. Finally, the Generation textfield shows the generation that is about to execute; if you press the Step button, the generation shown will execute. At present the simulation is paused prior to the execution of `initialize()` callbacks, a special initialization state that happens first before the simulation begins to run.

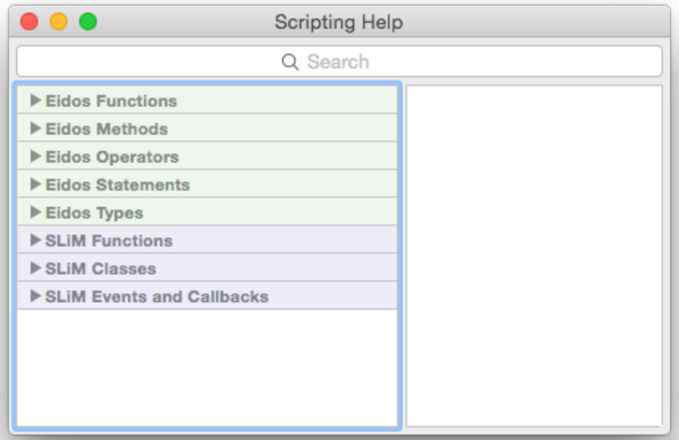
6. The color controls. The two color stripes show the colors that will be used by SLiMgui to indicate different fitness values (for individuals) and different selection coefficients (for mutations). In both cases, yellow is always neutral, but the scale of the color ramps around yellow can be adjusted using the vertical sliders to the right, in order to make the color scale better reveal fine or coarse differences in fitness and selection coefficients in your simulation.

7. The chromosome views. The two wide stripes show views onto the simulated chromosome (empty at present since the simulation has not yet started); these will be discussed later. To the right of those views are buttons for six commands. In the top row are buttons for Add Genetic Command (a pop-up menu button) and Show Details (a toggle button that shows and hides a drawer). Below those is a cluster of four buttons labeled R, G, M, and F; these toggle visibility on and off in the chromosome views of, respectively, rate maps (for recombination and mutation), genomic elements, mutations, and fixed mutations (i.e., substitutions). By default only mutations are shown.

This is a lot of information, and to avoid drowning you in details we will not cover all these elements in detail now; you will see them again later as they come up in context.

3.2 The script help window

Before moving on to writing your first Eidos script for SLiM, there are a few other components of SLiMgui that it might be useful to briefly mention. One such is the script help window. If you click the Script Help button ?, the script help window will open:

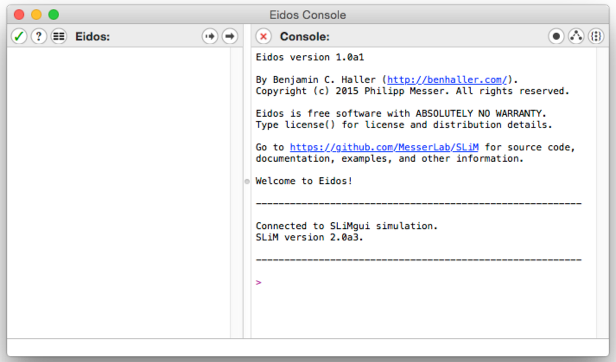


This window can be used to browse information about both Eidos and SLiM. A list of top-level topic headings appears on the left; you can click on these headings to expand them to show the sub-headings they contain, which may in turn be expanded to show sub-sub-headings and so forth. When you click on a "leaf" – an actual topic – the information about that topic will be shown in the pane on the right. You can also use the search field at the top of the window to search for information about a given topic; note that there is a pop-up menu under the magnifying glass that allows you to choose whether the search is done on topic titles only (for fewer and probably more relevant results), or is done on the full help text of each topic (for more results).

A useful shortcut: option-click on anything in the Eidos script of the simulation window's input area to pop up the script help window with search results for the item you option-clicked. This is very useful for quickly looking up functions, language keywords, and other such topics.

3.3 The Eidos console

Clicking the Show Eidos Console button ⊳ will show the console (or hide it, if already open):

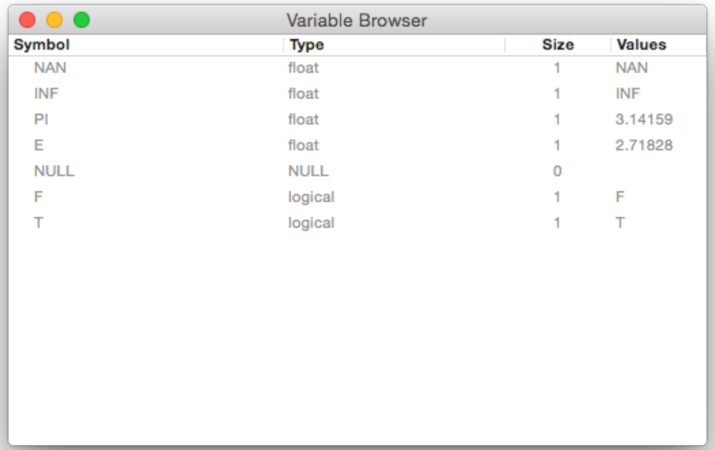


```
Eidos version 1.0a1

By Benjamin C. Haller (http://benhaller.com/).
Copyright (c) 2015 Philipp Messer. All rights reserved.

Eidos is free software with ABSOLUTELY NO WARRANTY.
Type license() for license and distribution details.

Go to https://github.com/MesserLab/SLiM for source code,
documentation, examples, and other information.

Welcome to Eidos!

---------------------------------------------------------

Connected to SLiMgui simulation.
SLiM version 2.0a3.

---------------------------------------------------------

>
```

We won't go into detail about this now, since you are not yet familiar with Eidos at all, but in essence, this console is a window where you can execute arbitrary Eidos commands at any point in your simulation. Commands are entered, and their output is shown, in the console pane on the right-hand side of the window. The left-hand side is a scratch area where you can work on longer blocks of script. If you want to experiment with Eidos and try out ideas interactively, this is the place to do it; so as new Eidos concepts are introduced in this manual, you may wish to return to the Eidos console to play around with them.

3.4 The Eidos variable browser

Finally, clicking the Show Eidos Variable Browser button ☷ will show (or hide, as appropriate) a variable browser that looks like this:


Variable Browser

Symbol	Type	Size	Values
NAN	float	1	NAN
INF	float	1	INF
PI	float	1	3.14159
E	float	1	2.71828
NULL	NULL	0	
F	logical	1	F
T	logical	1	T

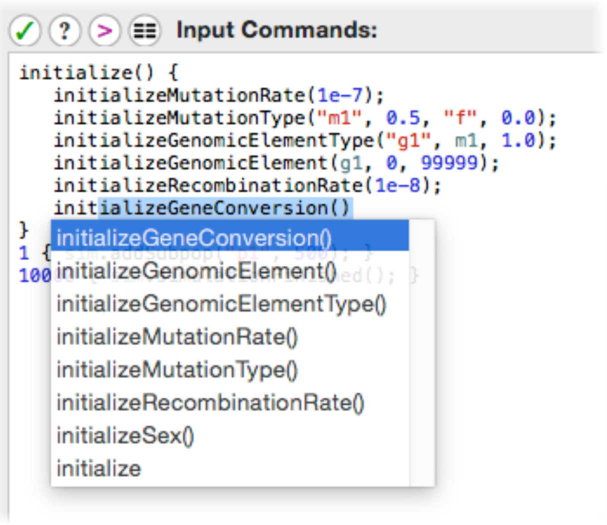
Only a few variables are presently defined; these are all constants – unmodifiable values defined for your use by Eidos (or by SLiM, but the constants shown are all Eidos constants). These constants include the values `T` and `F` representing true and false, the values `PI` and `E` representing those mathematical constants (`3.1415...` and `2.7182...`), and some others; these will be discussed as they come up.

Constants are shown in gray in the variable browser since they are unmodifiable. The variable browser will also show variables that you define yourself (in black rather than gray). For example, you might try now entering `x=10` at the console prompt in the Eidos console window. After you press return to execute that command, you will see the variable `x` appear in the variable browser, defined with a type of `integer`, a size of `1` (because `10` is a single value, as opposed to a vector of values), and a value of `10`.

We will return to the variable browser in later sections to examine some of the objects defined by SLiM. In general, however, just be aware that the variable browser exists, and that you can use it to examine all of the Eidos variables that you will be working with in later sections.

3.5 Automatic code completion and command syntax lookup

In the next chapter, we will start exploring a simple neutral model in SLiM. As you start writing scripts like that, you will sometimes find it difficult to remember the name of something you need to use in your script – a function, a property, or a method. We are getting a bit ahead of ourselves, but there is a final feature of SLiMgui to discuss here. Suppose you were writing a script, but you couldn't remember the name of the `initializeGeneConversion()` function. You could look it up in the documentation, but there is an easier way. First click in your script at the appropriate spot inside an `initialize()` callback, and then start typing with `init` since you know you're looking for an `initialize...()` function. Now press the `<esc>` key. This requests *code completion* from SLiMgui. In response, you should see something like this:

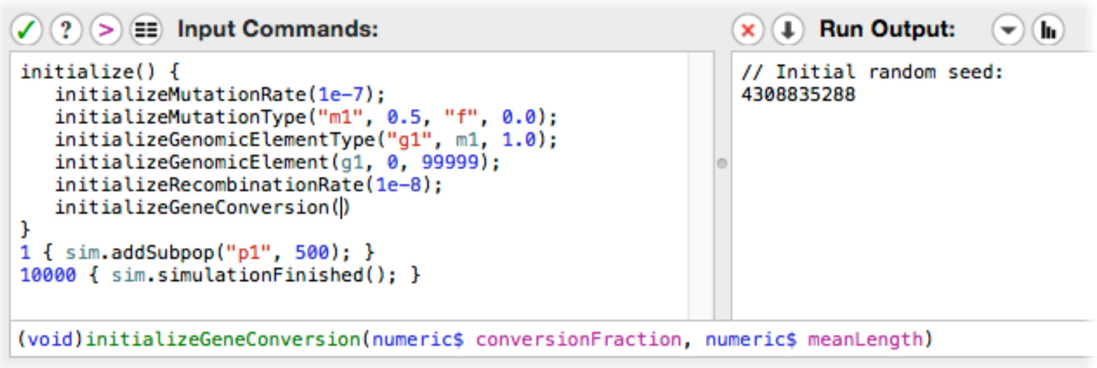


```
initialize() {
   initializeMutationRate(1e-7);
   initializeMutationType("m1", 0.5, "f", 0.0);
   initializeGenomicElementType("g1", m1, 1.0);
   initializeGenomicElement(g1, 0, 99999);
   initializeRecombinationRate(1e-8);
   initializeGeneConversion()
}
```

initializeGeneConversion()
initializeGenomicElement()
initializeGenomicElementType()
initializeMutationRate()
initializeMutationType()
initializeRecombinationRate()
initializeSex()
initialize

This is a pop-up list of all of the things Eidos knows about that start with `init`. Conveniently, `initializeGeneConversion()` is even selected for you, since it happens to be alphabetically first in the list. You can simply press return or click outside the box to accept the default choice; you could also double-click a different choice, or use the arrow keys to move to a different choice.

Having accepted `initializeGeneConversion()` as your choice, you might now also be unable to remember what its parameters are. Simply click between the parentheses of the function call, and then look at the status bar at the bottom of the window:



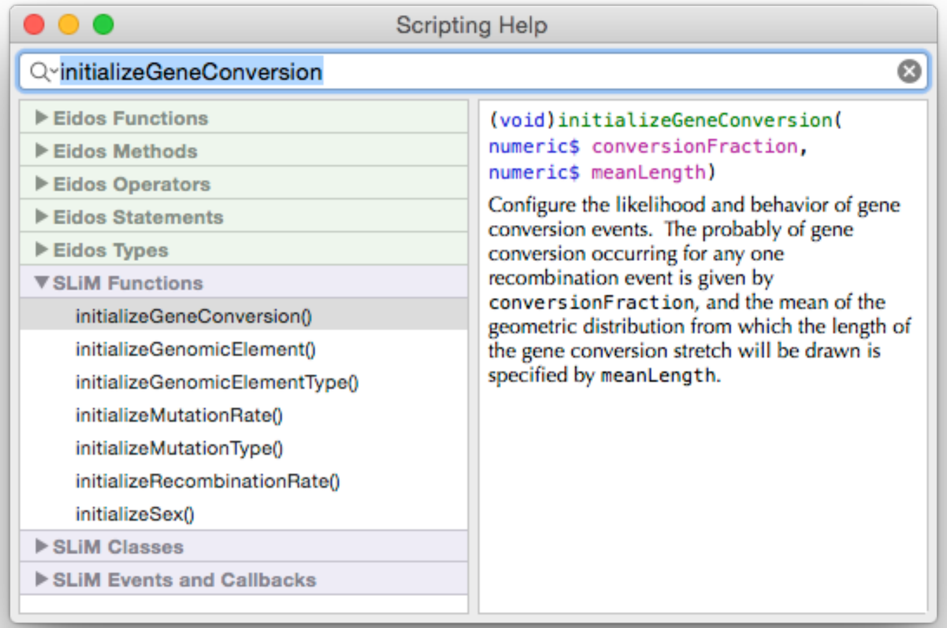
```
initialize() {
   initializeMutationRate(1e-7);
   initializeMutationType("m1", 0.5, "f", 0.0);
   initializeGenomicElementType("g1", m1, 1.0);
   initializeGenomicElement(g1, 0, 99999);
   initializeRecombinationRate(1e-8);
   initializeGeneConversion()
}
1 { sim.addSubpop("p1", 500); }
10000 { sim.simulationFinished(); }
```

```
// Initial random seed:
4308835288
```

```
(void)initializeGeneConversion(numeric$ conversionFraction, numeric$ meanLength)
```

The function signature shown there reminds you of the parameters needed, including their types and their names. Section 4.1.3 has further discussion about this feature, getting into details of the structure and symbolism of the function signature, which would have little meaning before we have started scripting.

As described in section 3.2, there is a script help facility provided in SLiMgui, which can be called up with an option-click on any part of your script. If the function signature shown above is not sufficient to jog your memory, and you want to see the full documentation for the `initializeGeneConversion()` function, just option-click on the function name, `initializeGeneConversion`, and the script help window will come up showing the results of a search on that term:



```
(void)initializeGeneConversion(
numeric$ conversionFraction,
numeric$ meanLength)
```

Configure the likelihood and behavior of gene conversion events. The probably of gene conversion occurring for any one recombination event is given by `conversionFraction`, and the mean of the geometric distribution from which the length of the gene conversion stretch will be drawn is specified by `meanLength`.

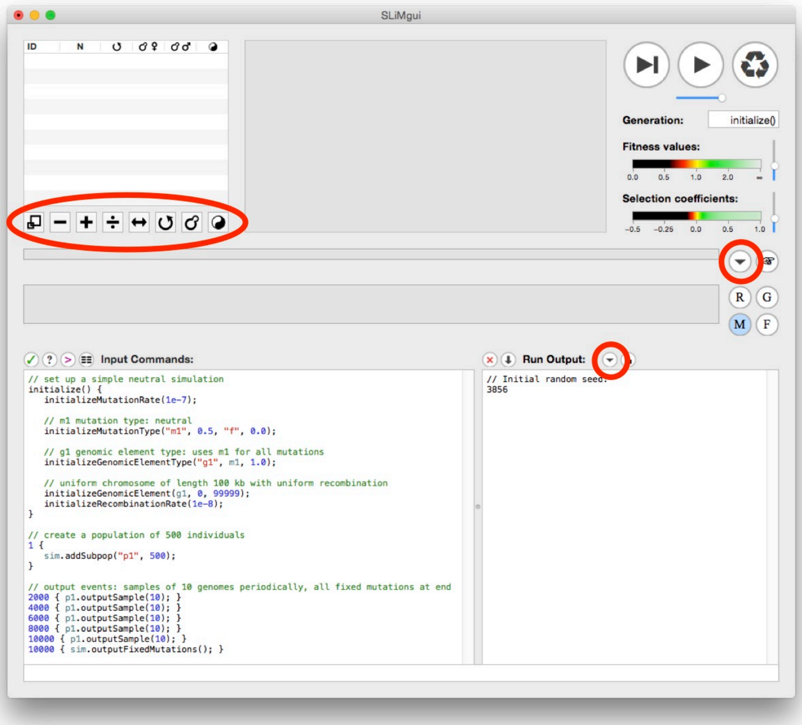
The full documentation for `initializeGeneConversion()` is shown, which should clarify any outstanding questions.

The code completion (with `<esc>`) and context help (with option-click) features work for properties and methods as well. This may not mean much to you yet, since functions, properties, and methods have not yet been formally introduced, but keep all this in the back of your mind as you start exploring scripting in chapter 4.

3.6 Automated script generation

In section 3.1, a few controls were skimmed over with a promise that they would be covered in later sections. Here we will cover some of those controls: various buttons and pop-up menus that add automatically generated script blocks to the simulation.

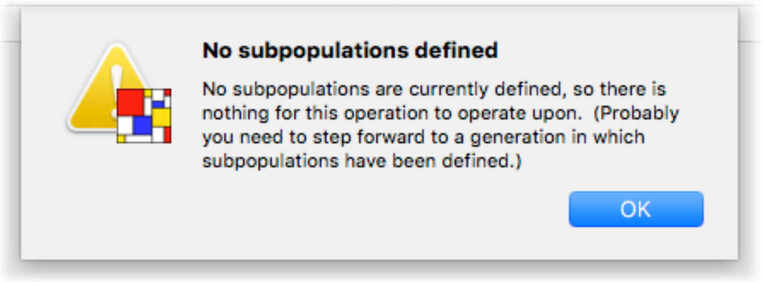
SLiMgui provides quite a few different facilities for automated script generation. Through the buttons under the subpopulation table, you can change the size of a subpopulation, remove or add subpopulations, split subpopulations, change migration rates, change selfing and cloning rates, or change a subpopulation's sex ratio. Through the pop-up menu to the right of the chromosome view, you can define a new mutation type or genomic element type, add a genomic element or a recombination interval to the chromosome, or make your simulation sexual rather than hermaphroditic (and even simulate a sex chromosome rather than an autosome). Finally, through the pop-up menu at the top of the Run Output area, you can add output of the full population state, output of a sample from a subpopulation, or output of a list of fixed mutations. You can see these three access points for automated script generation in the screenshot below:



```
// set up a simple neutral simulation
initialize() {
   initializeMutationRate(1e-7);

   // m1 mutation type: neutral
   initializeMutationType("m1", 0.5, "f", 0.0);

   // g1 genomic element type: uses m1 for all mutations
   initializeGenomicElementType("g1", m1, 1.0);

   // uniform chromosome of length 100 kb with uniform recombination
   initializeGenomicElement(g1, 0, 99999);
   initializeRecombinationRate(1e-8);
}

// create a population of 500 individuals
1 {
   sim.addSubpop("p1", 500);
}

// output events: samples of 10 genomes periodically, all fixed mutations at end
2000 { p1.outputSample(10); }
4000 { p1.outputSample(10); }
6000 { p1.outputSample(10); }
8000 { p1.outputSample(10); }
10000 { p1.outputSample(10); }
10000 { sim.outputFixedMutations(); }
```

```
// Initial random seed:
3856
```

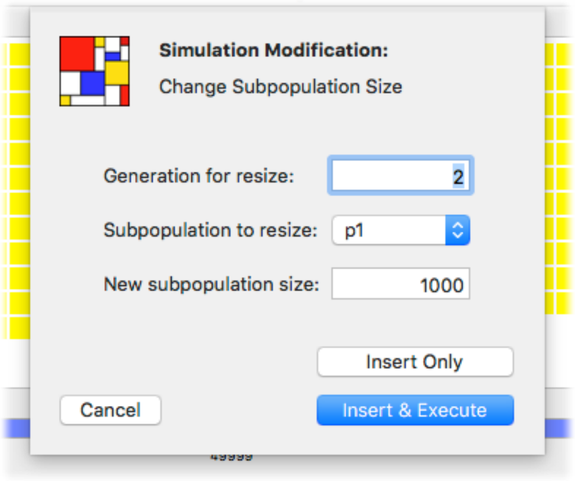
All of these automated script generation commands will not be covered individually here, as that would be too repetitive and tedious. The buttons have tooltips (visible if you hover the cursor over them), and the menu items are named in a way that indicates their function, so you can easily find the command you need. All of these commands work in essentially the same way, so we will take just one of them as a representative example. The leftmost button under the subpopulation table is the Change Subpopulation Size button. If you recycle and click it, you will likely see something like this:



No subpopulations defined

No subpopulations are currently defined, so there is nothing for this operation to operate upon. (Probably you need to step forward to a generation in which subpopulations have been defined.)

This illustrates the first point about SLiMgui's automated script generation: it depends upon the current state of the simulation. Immediately after doing a Recycle, no subpopulations have been defined in the current simulation, and so SLiMgui has no information about which subpopulations exist (and thus might be resized). The first step in using these facilities is therefore to get yourself into a state in which SLiMgui has enough information to make modifications to the objects you are interested in. In this example (using SLiMgui's default model), stepping forward twice (once to execute the `initialize()` callback, and another to execute the generation `1` event that defines subpopulation `p1`) provides that information. Now if you click the Change Subpopulation Size button, you should see a more useful panel:



Generation for resize: 2
Subpopulation to resize: p1
New subpopulation size: 1000

Other automated-script-generation panels will differ in their specifics, but the idea is always the same: you supply the information needed for the script generation, and then you either do an Insert Only operation (generating the script block but leaving the current state of the simulation unchanged) or you do an Insert & Execute operation (generating the script block and putting it into effect in the current simulation). In this case, suppose we enter a value of 5 for “Generation for resize”, and then click “Insert & Execute”. The first thing you will note is that a new script block has been inserted into your script by SLiMgui:

```
5 {
    p1.setSubpopulationSize(1000);
}
```

This simply implements the requested change using an Eidos event. The other thing you will notice is that this event is active in the current simulation, with no need to recycle. If you step forward through generation `5`, subpopulation `p1` will resize to `1000` individuals as requested (see section 5.1.1 for a proper introduction to the `setSubpopulationSize()` method). This allows you to develop the dynamics of a simulation as you go, adding events one by one without needing to recycle and step forward to see the effects of each event added.

If you choose a generation for the event that is prior to the next generation to be executed, SLiMgui will display a warning that the event cannot be executed in the current simulation (because its target generation has already come and gone, and it is not possible to modify the past simulation state retroactively). In this case, the Insert & Execute button will change to Insert & Recycle, so that you easily restart the simulation with the new event in effect.

Finally, it is worth noting that the automated script generation always provides you with a new event or callback, even if the command could be merged into an existing event or callback. For example, if we use the Add Mutation Type command to make a new `m2` mutation type (see section 4.1.3), we will get a new `initialize()` callback like this:

```
initialize() {
    initializeMutationType(2, 0.5, "f", 0.5);
}
```

Almost certainly, you will want to copy the call to `initializeMutationType()` into your main `initialize()` callback and delete the extra callback provided by SLiMgui; it is quite unusual to actually want to have more than one `initialize()` callback in a script, although it is legal. SLiMgui can’t guess exactly where the call ought to be inserted, however, so it leaves that to you.

3.7 Script prettyprinting

As you start writing your own scripts in SLiMgui, you may find that they look a bit raggedy because their line indentation doesn't follow standard coding conventions, like this:

```
initialize() {
    initializeMutationRate(1e-7);
      initializeMutationType("m1", 0.5, "f", 0.0);
      initializeGenomicElementType("g1", m1, 1.0);
         initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
subpopCount = 5;

            for (i in 1:subpopCount)
sim.addSubpop(i, 500);
    for (i in 1:subpopCount)
         for (j in 1:subpopCount)
         if (i != j)
         sim.subpopulations[i-1].setMigrationRates(j, 0.05);
}
10000 late() {
sim.outputFull();
}
```

This is a contrived example (based on the recipe in section 5.3.2), but you really will find that your script indentation starts to suffer as you change the structure of your code, moving code from block to block, wrapping some code in loops and unwrapping other code, and so forth. Indentation issues can make your code hard to read and maintain, but manually fixing the indentation of each line is a hassle. Instead, you can just use SLiMgui's automatic script prettyprinting facility. Select "Prettyprint Script" from the Script menu, or click the button just above the scripting pane, and your code will be reformatted:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    subpopCount = 5;

    for (i in 1:subpopCount)
      sim.addSubpop(i, 500);
    for (i in 1:subpopCount)
      for (j in 1:subpopCount)
         if (i != j)
            sim.subpopulations[i-1].setMigrationRates(j, 0.05);
}
10000 late() {
    sim.outputFull();
}
```

Only the line indentation is changed; all other aspects of your coding style are preserved, including blank lines, brace style, spacing around operators, and so forth.

3.8 Further SLiMgui features

SLiMgui has many more features, but they won't make much sense until we have gotten into writing scripts. For future reference, here is a cross-reference to some sections that present more features of SLiMgui:

Running a simulation: section 4.1.9.
Viewing script block registration/deregistration: section 5.1.2.
Executing a simulation up to a specified generation: section 5.1.2.
Visualizing population structure and migration: sections 5.1.3 and 5.3.3.
Using the Play speed slider: section 5.2.2.
Viewing recombination regions: section 6.1.1.
Viewing the sex ratio, cloning rate, and selfing rate: sections 6.2.2, 6.3.1, and 6.3.2.
Viewing the registered mutation types and their distributions of fitness effects: section 7.1.
Viewing the registered genomic element types: section 7.2.
Viewing genomic elements and selecting a subrange of the chromosome: section 7.3.
Customizing display colors for mutations, genomic elements, and individuals: section 7.4.
Graphing of mutation and population dynamics in SLiMgui: chapter 8.
Alternative population display modes: section 12.3.
Haplotype display in the chromosome view, and haplotype plots: section 13.5.

Finally, note that SLiMgui knows the recipes presented in this cookbook, and can open them for you directly. Just choose the recipe you want from the "Open Recipe" menu under SLiMgui's File menu, and the recipe will open in a new SLiMgui window.

4. Getting started: Neutral evolution in a panmictic population

This chapter will introduce the basic concepts involved in making, configuring, running, and obtaining output from a simple neutral simulation.

4.1 A basic neutral simulation

There is a tradition in computer programming of introducing a new language by writing a "hello, world" program. In Eidos, this minimal "hello, world" program is quite simple:

```
print("hello, world");
```

This single-line program calls a built-in function named `print()`, which prints whatever you tell it to. Here, `print` is called with a single argument, the string `"hello, world"`, enclosed in quotes that indicate it is a string. The semicolon at the end indicates to Eidos that the statement – the line of code – ends at that point. If you are using SLiMgui on OS X, you can open the Eidos console window now and enter this command at the prompt; after you press return, `"hello, world"` will be shown as output. In SLiM, we use Eidos as a tool for building and controlling SLiM simulations; for a complete introduction to Eidos, see the manual *Eidos: A Simple Scripting Language*.

That was a minimal Eidos program; now let's look at a minimal SLiM simulation script, which is a bit more involved. We'll start with a basic neutral simulation that models a genomic region of length 100 kb in a population of 500 diploid individuals, evolving over 10000 generations. Neutral mutations occur uniformly in this region at a rate of 10^{-7} per bp per generation. Recombination also occurs uniformly at a rate of 10^{-8} per bp per generation (corresponding to 1 cM/Mbp). The Eidos commands for specifying this simulation are as follows:

```
// set up a simple neutral simulation
initialize()
{
    // set the overall mutation rate
    initializeMutationRate(1e-7);

    // m1 mutation type: neutral
    initializeMutationType("m1", 0.5, "f", 0.0);

    // g1 genomic element type: uses m1 for all mutations
    initializeGenomicElementType("g1", m1, 1.0);

    // uniform chromosome of length 100 kb
    initializeGenomicElement(g1, 0, 99999);

    // uniform recombination along the chromosome
    initializeRecombinationRate(1e-8);
}

// create a population of 500 individuals
1
{
    sim.addSubpop("p1", 500);
}

// run to generation 10000
10000
{
    sim.simulationFinished();
}
```

Running this script at the command line on a Un*x system (including Mac OS X) is very simple. If it is saved in the current directory as a file named `test.txt`, and if the `slim` command-line tool is in the shell's executable path, then the command:

```
slim test.txt
```

should suffice to run it. Otherwise, paths will be needed, which depend upon where the `slim` command-line tool and the `test.txt` file are located. On OS X, the SLiM installer will install `slim` in `/usr/local/bin`; if `test.txt` is in your home directory, then the command would be:

```
/usr/local/bin/slim ~/test.txt
```

Running this script in the SLiMgui application on OS X is also straightforward. Just launch SLiMgui (installed in `/Applications` by the SLiM installer), copy/paste the script into the script area of SLiMgui's window (or, even easier: select the section 4.1 recipe from the Open Recipe submenu of SLiMgui's File menu), press the big Recycle button at the upper right of the window to reset the simulation with the new script, and then press the Play button just to the left of the Recycle button. Chapter 3 provided a brief introduction to SLiMgui and the parts of its window, and the sections below will walk through running this particular simulation in SLiMgui in more detail.

There are a couple of general things to say first about the whole script. First of all, comments in Eidos begin with two slashes, `//`, and continue to the end of their line; the script above has a comment for most of the lines of executable code.

Second, this code snippet utilizes syntax coloring to make the meaning of the script clearer, just as shown in SLiM's input area. Numeric constants are shown in blue, string constants in red, SLiM object constants such as `m1`, `g1`, and `sim` in sage, and comments in green. Syntax coloring will generally be used in this manual for Eidos scripts.

Third, braces `{}` are used in Eidos to enclose whole blocks of code. The code above has three such blocks: an `initialize()` callback that sets up the simulation, an Eidos event that is set to execute in generation `1` – the beginning of simulation execution – to add a subpopulation, and an Eidos event that runs in generation `10000` and stops the simulation.

Fourth, whitespace such as spaces, tabs, and newlines is not generally significant in Eidos; comments, also, are considered whitespace and do not matter to the execution of your code. The above script could thus be written more compactly as:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
10000 { sim.simulationFinished(); }
```

With that prelude, the following subsections will explore each of the commands in this script in detail. If you wish to following along in SLiMgui, you should copy the example script out of this document and paste it into your SLiMgui simulation window, then press the Recycle button (which abandons the previous simulation run, based on the old script, and begins a new simulation based on the new script you have just pasted in).

4.1.1 `initialize()` callbacks

Before a simulation can really begin running, some initialization tasks need to be done. SLiM needs to know basic simulation parameters like the mutation rate, the length of the chromosome, and so forth. Setting up this foundational state is done before the execution of the first generation, at what is called "initialization time". At initialization time, SLiM calls any blocks in your script that are designated as `initialize()` callbacks (simply by having `initialize()` before their starting brace). Our sample script defines one `initialize()` callback; you are allowed to have more than one, in which case they are called sequentially in the order in which they are defined in the script. This would be useful mostly for conceptual division of your code into discrete sections.

An `initialize()` callback may contain arbitrary Eidos code; you can define variables, execute loops, and call functions (all topics we will explore in future sections). However, the simulation is not yet set up, so you do not have access to SLiM's `sim` constant, and this cuts you off from most of SLiM's functionality. Mostly what you will do in your `initialize()` callbacks, in practice, is call initialization functions that are built into SLiM to help set up your simulation. These functions have names that begin with the word `initialize`; the `initialize()` callback here calls five such functions, discussed in the following sections. (A full reference of all of the `initialize...()` functions provided by SLiM is given in Part II of this manual, the reference section; in general all of the topics discussed in Part I are summarized in a more reference-oriented format there).

4.1.2 Mutation rate

The first line of our `initialize()` callback is:

```
initializeMutationRate(1e-7);
```

This calls the SLiM function `initializeMutationRate()`, passing a single parameter, the numeric constant `1e-7`. This is written in a sort of scientific notation commonly used in programming; `1e-7` means 1.0×10^{-7}, and could also be written in Eidos as `0.0000001`. Numeric values in Eidos may be of type `integer`, like `6` or `-17`, or of type `float`, like `1e-7` or `0.0000001`.

The effect of this statement is to tell SLiM that the simulation will use a uniform mutation rate of `1e-7` (per base position per generation) across the whole chromosome. SLiM uses this rate to determine how many mutations arise in each offspring that it generates in each generation in the genomic elements being simulated (see section 21.1 for a more precise definition of the mutation rate in SLiM). It is also possible to set a mutation rate map that varies the mutation rate along the chromosome, but we will defer that until later. Precisely what mutations can arise in a given element is governed by other aspects of the simulation configuration, discussed next.

4.1.3 Mutation types

The next line in the `initialize()` callback is:

```
initializeMutationType("m1", 0.5, "f", 0.0);
```

This calls the SLiM function `initializeMutationType()` to set up a new mutation type. You may define as many mutation types in SLiM as you wish. Each is given a unique symbolic name; the mutation type defined here is given the name `m1`, as requested by the first parameter to the function call. A mutation type encapsulates a few key pieces of information about a particular type of mutations: the dominance coefficient for mutations of this type (`0.5` here), the distribution of fitness effects (DFE) to be used (a fixed fitness effect here, as represented by `"f"`), and any parameters that configure the distribution of fitness effects (`0.0` here, giving the fixed selection coefficient that will be used by all mutations of this type). This call creates a new Eidos variable named `m1`, and so henceforth we can use the symbol `m1` to refer to this mutation type.

This mutation type, `m1`, thus represents neutral mutations – always with a selection coefficient of `0.0`. Mutation types might represent things like neutral mutations, beneficial mutations, deleterious mutations, nearly neutral mutations, etc., with different distributions of fitness effects. Each time that a mutation is created, its selection coefficient is drawn from the distribution of fitness effects specified by the mutation type to which the new mutation belongs. It can be useful to use different mutation types to represent mutations that are conceptually different in your simulation even if they share the same DFE. For example, you might use mutation type to represent neutral mutations created by SLiM randomly as a result of normal mutational processes, and a different mutation type with exactly the same DFE to represent a particular neutral mutation that you deliberately create in your script and want to track separately during the simulation.

You might notice that it seems hard to remember what all four parameters are and which order they are supposed to go in. If you are using SLiMgui, a helpful feature is provided to address this problem (introduced in section 3.5, with a screenshot). If you click anywhere inside the parentheses of the `initializeMutationType()` call, a summary of the syntax of the call is shown in the status bar at the bottom of the window:

```
(object<MutationType>$)initializeMutationType(is$ id,
   numeric$ dominanceCoeff, string$ distributionType, ...)
```

The Eidos manual has a complete description of meaning of these summaries, called *function signatures*. Briefly, this function signature first gives the type of value returned by the function – here, an `object` value of class `MutationType`, representing the new mutation type created by the function call. This returned value is a *singleton*, meaning that there will be only a single value present, rather than a vector containing multiple values; this singleton property is represented by the trailing `$`. You could therefore assign the result of `initializeMutationType()` into a variable:

```
x = initializeMutationType("m1", 0.5, "f", 0.0);
```

This would define `x` to refer to the new mutation type. Since the variable `m1` is defined automatically with the same value, this is usually not necessary; you would use `m1` to refer to the new mutation type. In some cases, however, it can be useful, particularly if you are defining more than one mutation type using a loop.

Now we get to the parameters listed in the function signature. The first parameter may be either an `integer` or a `string` (thus the designation `is`, from the leading character of each permitted type name). This parameter should be a singleton, and is named `id`; it gives the identifier to be used for the new mutation type, either as an integer like `1` or as a string like `"m1"` (both of which would lead to a variable named `m1` being defined). The second parameter must be `numeric` (meaning either an `integer` or a `float`), is a singleton, and is named `dominanceCoeff`; this is self-explanatory. The third parameter must be a singleton `string`, and is named `distributionType`. Then there is `...`, a signifier that zero or more additional parameters might be supplied of unspecified type and name. In the case of `initializeMutationType()`, these additional parameters configure the distribution of fitness effects (DFE), and their number and type depend upon the distribution specified by `distributionType`. Exponential, gamma, and normal DFEs are also supported by SLiM, for example, and require different parameters for their specification; consult the reference manual for details about all of the DFE types currently supported in SLiM.

For now, the overall point is that the function signature is always available in the status bar whenever you click inside a function, and can be used as a quick reference to remind you of the meaning and type of each parameter. Remember that in SLiMgui you can also option-click in Eidos code to bring up the script help window showing a search on the clicked term (see section 3.5); an option-click on `initializeMutationType` would bring up not only the function signature for the function, but the full text from the reference section regarding the function. You might try this now, as an experiment.

4.1.4 Genomic element types

Let's now turn to the third line of the `initialize()` callback:

```
initializeGenomicElementType("g1", m1, 1.0);
```

This creates a new genomic element type named `g1`. A genomic element type represents a particular type of chromosomal region – introns, exons, UTRs, etc. As with mutation types, you might wish to use a special genomic element type for a particular chromosomal region that you want to track separately in your simulation, even if it has the same characteristics as other similar regions – an exon of particular interest, for example.

Each genomic element type has a particular mutational profile. Mutations occur in all genomic elements at the same uniform rate, as set by the overall mutation rate; but the types of mutations that can occur in a particular genomic element type are determined by the mutational profile of that genomic element type. Here, genomic element type `g1` is defined as using mutation type `m1` for all of its mutations (as specified by the proportion `1.0` supplied as the third parameter).

Suppose we wanted to define `g1` as using a mix of three mutation types, `m1`, `m2`, and `m3`? Let's look at the function signature for `initializeGenomicElementType()` to see how we might do this:

```
(object<GenomicElementType>$)initializeGenomicElementType(is$ id,
   io<MutationType> mutationTypes, numeric proportions)
```

In some ways this is quite similar to the function signature for `initializeMutationType()` that we examined above; it returns an `object` (this time of class `GenomicElementType`), and it takes an `integer` or `string` named `id` to specify the identifier for the new object. The second parameter is named `mutationTypes`, and can be either of type `integer` or `object` (with class `MutationType`); so we could specify the mutation type for the genomic element type either using an object like `m1`, as we did in the example script, or using an integer like `1` (identifying mutation type `m1`), which might be more convenient. The third parameter is of type `numeric` (`integer` or `float`, remember) and specifies the proportion of all mutations that will be drawn from the given mutation type.

The second and third parameters are not designated as singletons (they do not have a `$` in their type specifier). This means that they can be *vectors* of values, which allows us to specify multiple mutation types for a genomic element type:

```
initializeGenomicElementType("g1", c(m1,m2,m3), c(1,2,10));
```

The `c()` built-in function returns all of its parameters pasted together into a single vector; we use it here to make a vector containing the three mutation types, and another vector containing proportions. Notice the proportions don't have to sum to `1`; they are just relative proportions.

In Eidos, *all* values are in fact vectors; singletons are just vectors containing exactly one value. Even when you write a numeric constant like `10`, that is actually an Eidos vector that happens to be a singleton. Many Eidos operators and functions are built to work with whole vectors; this simplifies your code by removing the need for many of the loops that would be necessary in other languages in order to loop over the elements in an array. It also makes Eidos much faster, since a whole vector can be processed in a single statement. For example, take this Eidos statement:

```
sum(1:10);
```

This adds the numbers from `1` to `10` using the built-in `sum()` function. A vector containing the numbers from `1` to `10` is generated using the sequence operator of Eidos, `:`, which counts upwards (or downward) from its first operand to its second operand. Once you get used to the way vectors work in Eidos, you will find that they often make complicated tasks very easy.

4.1.5 Genomic elements

Having set up genomic element type `g1` in the third line, the fourth line of the `initialize()` callback now uses `g1` to set up a genomic element:

```
initializeGenomicElement(g1, 0, 99999);
```

A genomic element is simply a region of the chromosome that uses a particular genomic element type. For example, you might have one genomic element type that represents introns, and you might then have dozens (or thousands) of genomic elements in your chromosome that use that genomic element type to represent a specific intron at a particular position. The call here sets up a single genomic element that stretches from base position `0` to base position `99999`, and is thus `100000` bases long, using genomic element type `g1`.

A chromosome can consist of many genomic elements, but two genomic elements cannot overlap. Genomic elements also do not have to cover the entire chromosome. For example, you can run a simulation with only two genomic elements of length 1 kb each, separated by 50 kb of "empty space". Mutations are only simulated in those regions of the chromosome where a genomic element has been specified. Recombination events, however, are still simulated across the whole chromosome. The end position of the last genomic element determines the length of the chromosome being simulated. You can see the genomic elements you have defined by turning on the display of genomic elements in SLiMgui's chromosome view (see section 3.1).

The following example shows how we can set up a chromosome consisting of ten genomic elements of type `g1`, with gaps between them at regular intervals:

```
for (index in 1:10)
    initializeGenomicElement(g1, index*1000, index*1000 + 499);
```

This introduces a few new Eidos concepts. First of all, `1:10` makes a vector containing the sequence from `1` to `10`, as we saw above; it is equivalent to `c(1,2,3,4,5,6,7,8,9,10)`.

Second, the `for`...`in` construct loops over that vector; for every value in `1:10`, the value will be assigned to the variable `index` and then the body of the loop – the statement on the next line – will be executed. In this way, `initializeGenomicElement()` will be called ten times, first with `index` equal to `1`, then with `index` equal to `2`, and on up to `index` equal to `10`.

Third, you can see that Eidos, like most programming languages, allows you to write mathematical expressions that are evaluated when the script executes. The `*` operator indicates multiplication and the `+` operator indicates addition, so the expressions here calculate start and end positions based upon the current value of `index`. All in all, this `for` loop is essentially equivalent to:

```
initializeGenomicElement(g1, 1000, 1499);
initializeGenomicElement(g1, 2000, 2499);
...
initializeGenomicElement(g1, 10000, 10499);
```

It should now be fairly obvious how one might extend the `for` loop above to create a much more complex chromosome involving multiple genes, each with UTRs and introns and exons, interspersed with non-coding regions, and so forth. You would likely want to use additional features of Eidos that are described in the Eidos language manual, such as nested `for` loops and the modulo operator `%`. You could also potentially read in a chromosome map from a file on disk, parse that map in whatever format it is written in, and execute the corresponding commands to build the map in Eidos; Eidos has all of the tools you would need to do this, including file input/output and string processing.

4.1.6 Recombination rate

The final line of the `initialize()` callback in our script is:

```
initializeRecombinationRate(1e-8);
```

This specifies the recombination rate for the whole chromosome to be `1e-8`, which means that a crossing-over event will occur between any two adjacent bases with a probability of `1e-8` per genome per generation (see section 21.1 for a more precise definition of the recombination rate in SLiM). In this case, a single recombination rate is used along the whole chromosome. The function signature for `initializeRecombinationRate()`, however, is:

```
(void)initializeRecombinationRate(numeric rates, [Ni ends = NULL],
    [string$ sex = "*"])
```

Parameters named `ends` and `sex` are listed; however, they are in brackets `[]`. This indicates that these parameters are optional and may be omitted (in which case they are assigned the default values shown in the signature; see the Eidos manual for further discussion of optional arguments). That is what we did in the example script, so `ends` was assigned its default value of `NULL` (and `sex` was assigned its default value of `"*"`, which we won't discuss here). If we included `ends`, which must be either `NULL` or an `integer` value according to its `Ni` type-specifier in the signature, then it should be the last base position of the chromosome, like this:

```
initializeRecombinationRate(1e-8, 99999);
```

Notice that the `rates` and `ends` parameters are not singletons (no `$`). In fact, we may supply a vector of end positions and a matching vector of rates, defining a series of recombination regions, each starting at the base position after the previous range ends (or at the beginning of the chromosome, for the first range). For a simple example, we could make the first half of the chromosome experience a much higher recombination rate than the second half:

```
initializeRecombinationRate(c(1e-7,1e-8), c(49999,99999));
```

You may supply as many recombination regions as you wish, specifying recombination hotspots, etc. These recombination regions are not related to genomic elements; the boundaries of recombination regions and genomic elements do not need to match up at all. You can see the recombination regions you have defined by turning on the display of recombination regions in SLiMgui's chromosome view (see section 3.1). Note also that recombination can be tailored on an individual-level basis using a `recombination()` callback to model things such as chromosomal inversions; see sections 13.5 and 21.5.

As mentioned in section 4.1.2, it is also possible to define a mutation rate map that varies the mutation rate along the chromosome. In fact, that is done with exactly the same syntax that we have just seen here to configure a recombination rate map; a vector of rates and end positions is supplied to `initializeMutationRate()` instead a singleton rate.

With this, we're done discussing the `initialize()` callback section of the script. After the `initialize()` callback finishes, the generation counter will be set to `1` and the first generation will be ready to execute, as discussed next. If you're following along in SLiMgui (which you can do by pressing the Step button in the simulation window once), the generation counter will change from `initialize()` to `1`, indicating that the initialization phase is done and generation `1` is next up to be executed (but has not executed yet). If you have the variables browser open (you can open it now if you wish), you will see that the variables `m1` and `g1`, defined by the `initialize()` callback, are now listed, along with another variable named `sim` that will be discussed below.

4.1.7 Eidos events

The next section of our script is:

```
1
{
    sim.addSubpop("p1", 500);
}
```

This defines an *Eidos event* that is scheduled to run in generation `1` – at the very beginning of the simulation, but after the `initialize()` callbacks have completed. This is the usual time at which new subpopulations are constructed, and that is what this event does, as will be discussed in the next section. For now, however, we're interested in this idea of defining Eidos events.

Eidos events are run at the beginning of each generation, by default, as shown in the generation schedule in section 1.3. Each event is scheduled to run in a specific generation or range of generations. A single generation is specified with a single number, as here. A range of generations is specified with the Eidos sequence operator; we could make an event run in generations 10 through 19, for example, by writing:

```
10:19 { ... }
```

The `...` here is the script for the event, of course; it can be whatever Eidos code you wish. We will see a great many Eidos events in later examples.

4.1.8 Subpopulations

The Eidos event scheduled to run in generation 1 has a single line in its body:

```
sim.addSubpop("p1", 500);
```

This looks a bit like a function named `sim.addSubpop()` is being called – and that is almost right, but not quite. After `initialize()` callbacks complete, SLiM defines a new Eidos constant named `sim` that represents the simulation itself. The `sim` object is used to access all sorts of simulation properties, as we will see later. It is also a sort of gateway for a specialized sort of function calls referred to as *methods*. A method is a call that can be made to a particular object, to request that that object perform some operation. All values of type `object` in Eidos support a handful of basic methods (as you can read about in the Eidos manual), and the `object` classes defined by SLiM often support several more specialized methods as well.

So here we call the `addSubpop()` method of the `sim` object. This adds a new subpopulation to the simulation; it will be represented by the new variable `p1`, as specified by the first parameter, and it will have an initial size of `500` diploid individuals (the second parameter). The individuals in the new subpopulation are blank slates; they contain no mutations as of yet. The method call is done using the member operator of Eidos, a period ("`.`"); this operator selects one member, such as a method, from an object. Apart from this syntactic difference, methods are in many ways quite similar to functions, but they encapsulate an "object-oriented" perspective; instead of a globally defined function performing an operation, a specific object is asked to perform the operation. Subpopulations "belong" to the simulation, and therefore the simulation – the `sim` object – is asked to add new subpopulations.

If you have been following in SLiMgui, you can now press Step again, and you will see that a new variable named `p1` appears in the variable browser to represent the new subpopulation. You might now open the Eidos console and enter `sim.methodSignature()`. This is a method that returns the signatures for all of the methods supported by an object. Among other methods in this list (all documented in the reference section of this manual), you will see the signature for `addSubpop()`:

```
– (object<Subpopulation>$)addSubpop(is$ subpopID, integer$ size,
    [float$ sexRatio = 0.5])
```

Notice there is a third parameter, which is optional, named `sexRatio`. This will be discussed when sexual simulations are covered in chapter 6. The dash at the very beginning indicates that the signature is for a method, as opposed to a function signature, which has no leading dash. Methods are sometimes referred to by name with this leading dash; the `addSubpop()` method is thus sometimes called `-addSubpop()`. The meanings are identical.

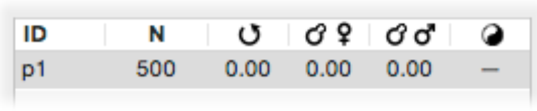
4.1.9 Executing the simulation

We have already executed the initialization phase and the first generation of the simulation (if you are following along in SLiMgui). Now try pressing the Play button. The simulation will suddenly run at full speed, which is probably pretty fast in this case. You will see mutations flicker in and out of existence, and rise and fall in frequency, along the length of the chromosome, as displayed in the chromosome views. If you let the simulation run, it will go until it reaches generation `10000`, at which point it will stop because of the final snippet of code in our example script:

```
10000
{
    sim.simulationFinished();
}
```

This defines an Eidos event that executes in generation `10000`. The event calls a method named `simulationFinished()` on the `sim` object, and that method declares that the simulation is finished (although it continues to execute until the end of the current generation). This is actually not the typical way that a simulation ends, as we will see in the next section; but it will serve for now. When the simulation stops, the generation counter will read `10001` because generation `10000` finished executing and the next generation to execute (were the simulation not finished) would be `10001`.

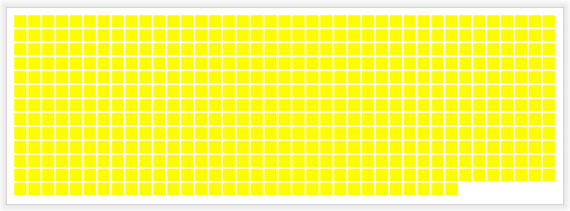
Having reached the end of the simulation, let's look at a few parts of the simulation window. The population table view now looks something like this:



ID	N	↺	♂♀	♂♂	◐
p1	500	0.00	0.00	0.00	–

This shows the subpopulation that the generation `1` Eidos event created, named `p1` as sown in the ID column, along with its size (`500`) and its selfing and cloning rates (all `0.00`). The last column shows the sex ratio (M:M+F); simulations in SLiM are hermaphroditic by default, so the sex ratio is undefined.

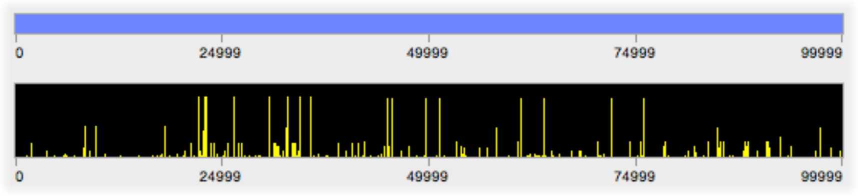
The individual view now looks something like this:



Each yellow square represents one individual; there are 500 squares since the subpopulation size is 500. Each individual is colored according to the calculated fitness of that individual;

however, in this simulation all mutations are neutral, so all individuals have the same relative fitness, 1.0, and so they are all yellow (as expressed by the color stripe for fitness values, discussed in section 3.1). In a simulation with beneficial and deleterious mutations you would see a range of colors, giving you an immediate visual sense of the fitness distribution across the subpopulation.

Finally, the chromosome view area looks something like this:



The top band shows the whole chromosome; the numbers and ticks below indicate base positions. You can click and drag here to select a subrange of the chromosome for display in the bottom view; a simple click in the top band will return you to viewing the full chromosome. The bottom band displays the selected range of the chromosome (here, the full range). Each yellow bar is a mutation that exists at that position in the chromosome. The height of the bar indicates the frequency of the mutation; if the bar reaches the full height of the band, it has reached fixation and is removed from the display (but you can turn on display of fixed mutations with the `F` button, in which case they will display as full-height blue bars, by default). Here, all the bars are yellow because all the mutations in this simulation are neutral, and neutral mutations are colored yellow as shown by the color stripe at upper right (see section 3.1).

You might have noticed that whole sets of yellow bars tend to rise and fall in synchrony. These are haplotypes that have become associated with each other through genetic drift. The dynamics of mutations, haplotypes, and genetic drift is immediately visually apparent here, underlining the value of having an interactive graphical interface in which you can develop, debug, test, and experiment with your simulations. This visual, interactive workflow also makes SLiMgui a potentially valuable tool for classroom instruction in population genetics and evolutionary biology.

4.2 Basic output

So far, our basic neutral simulation simply stops in generation 10000. Typically, it is desirable for a simulation to produce some output. We will look at a few output options in this section.

4.2.1 Entire population

One option is to output the full state of the population (i.e., all individuals in all subpopulations). To do this, we might change our script just a bit:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
10000 late() { sim.outputFull(); }
```

The only change here is that the final event, including the `sim.simulationFinished()` call, has been replaced by a different event to generate output using the `sim.outputFull()` method:

```
10000 late() { sim.outputFull(); }
```

Note the keyword `late()` here. SLiM can run user-defined Eidos events at two different points in the generational life cycle, as shown in section 1.3. These two points are referred to as `early()` and `late()` events. Events are `early()` by default, so the original line:

```
10000 { sim.simulationFinished(); }
```

defined an `early()` event, and could just as well have been written as:

```
10000 early() { sim.simulationFinished(); }
```

Most of the time, running events early in the generation, prior to the generation of offspring, is desirable (which is why that is the default). In some cases, however, it is better for an event to run toward the end of the generation, after the generation of offspring – and events that produce output are usually such a case. If the `late()` specifier were omitted, the output would be generated at the beginning of generation `10000`, instead of at the end, and would thus reflect the results of running the model for only `9999` generations. After the output was generated, the model would then run for the final generation, with no effect on the model's output.

That would be quite a subtle bug, and easy to miss. In fact, generating output at the beginning of a generation, in an `early()` event, is so likely to be a bug that SLiM will output a warning if you try to do it using one of SLiM's standard output generation methods. For example, if we delete the `late()` designation on the output event above, SLiM will generate a warning when the model executes:

```
#WARNING (SLiMSim::ExecuteInstanceMethod): outputFull() should probably
not be called from an early() event; the output will reflect state at the
beginning of the generation, not the end.
```

There are a few other common situations in which you want to use a `late()` event instead of the default `early()` events, most notably when you introduce new mutations into the simulation in script; these situations will be discussed as they arise.

Once you have copied and pasted this new script into your simulation window, press Recycle and then Play, and let the simulation run to the end. Notice that the full state of the population has been printed, as requested in an output section that looks something like this (with large chunks of output skipped over with ellipses):

```
#OUT: 10000 A
Populations:
p1 500 H
Mutations:
29 68306 m1 34640 0 0.5 p1 6848 450
2 68503 m1 7251 0 0.5 p1 6867 561
...
Individuals:
p1:i0 H p1:0 p1:1
p1:i1 H p1:2 p1:3
...
Genomes:
p1:0 A 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
p1:1 A 16 17 18 7 8 19 9 20 21 22 23 24 25 26 27 28
...
```

The format here is fairly simple and easily parsable by something like an R script; it can also be read by SLiM in order to read in a population from a saved state, as we will see later. It begins with an output prefix, `#OUT:`, followed by the generation (`10000`) and the type of output (`A` for all).

The next section describes the subpopulations; `p1` is of size `500` and is hermaphroditic (`H`).

Next comes a list of all mutations present; each line shows one mutation, including (1) a temporary unique identifier used only in this output section, (2) a permanent unique identifier kept by SLiM throughout a run, (3) the mutation type, (4) the base position, (5) the selection coefficient (here always 0 since this is a neutral model), (6) the dominance coefficient (here always 0.5), (7) the identifier of the subpopulation in which the mutation first arose, (8) the generation in which it arose, and (9) the prevalence of the mutation (the number of genomes that contain the mutation, where – in the way that SLiM uses the term "genome" – there are two genomes per individual).

Next comes a list of individuals. The first line of this section as shown above, for example, shows that individual `0` in subpopulation `1` (`p1:i0`) is a hermaphrodite (`H`) and is comprised of two genomes, `p1:0` and `p1:1`, that will be listed in the following section. This section makes it easier to figure out which genomes correspond to which individuals, but is largely redundant.

The final section lists all of the genomes in the simulation. The first line in this section as shown above, for example, shows that genome `p1:0` (which the Individuals section told us belonged to individual `p1:i0`) is an autosome (`A`) and contains the mutations with the identifiers `0`, `1`, `2`, ... `19`.

From all of this information, the complete state of the population can be reconstructed – every individual, and every mutation contained by every individual – thus the method name `outputFull()`.

4.2.2 Random population sample

Often the `outputFull()` method is overkill; you might just want a sample of genomes that is randomly drawn from a particular subpopulation. For example, to output a `10`-genome sample at the halfway point of the simulation, here is a modified script:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
5000 late() { p1.outputSample(10); }
10000 late() { sim.outputFull(); }
```

The only change relative to the previous script is the added line:

```
5000 late() { p1.outputSample(10); }
```

This calls the method `outputSample()` on the subpopulation from which the sample should be taken, `p1`, with a requested sample size of `10` genomes (not `10` individuals, note; `outputSample()` outputs randomly selected haploid genomes). If you copy and paste this script into SLiMgui, Recycle and Play, you will see that at generation `5000` some output appears:

```
#OUT: 5000 SS p1 10
Mutations:
21 203188 m1 92838 0 0.5 p1 4489 4
4 203247 m1 73991 0 0.5 p1 4495 6
...
Genomes:
p1:0 A 0 1 2 3 4 5 6
p1:1 A 0 7 1 3 4 5 8 6 9
...
```

The format here is very similar to that of `outputFull()`, but the header `#OUT: 5000 SS p1 10` indicates that in generation `5000` a sample (`S`) was taken from `p1` of size `10` genomes and was output in SLiM (`S`) format. The list of mutations and genomes is identical in format to `outputFull()`, except that only those mutations are shown that are actually present in the sample, and that prevalence now refers to the sample rather than the entire population. The list of populations and the list of individuals are also omitted in this output style.

SLiM also supports output of samples in MS format. The previous recipe can be modified to use the `outputMSSample()` method instead of the `outputSample()` method; running the recipe in SLiMgui would then produce MS-style output at generation `5000`:

```
segsites: 73
positions: 0.0262003 0.0351204 0.0445104 0.0597206 0.0647306 0.0702307
0.0871209 0.1039710 0.1046410 0.1162212 0.1222912 0.1407114 0.1608916
0.1728717 0.1775018 0.2036920 0.2366524 0.2462625 0.2468625 0.2475225
0.2531725 0.2858329 0.2880929 0.2913729 0.2998330 0.3045530 0.3048630
0.3132831 0.3279533 0.3400434 0.3484835 0.3544035 0.3547335 0.3586336
0.3594236 0.3765438 0.3845438 0.4385444 0.4441644 0.4460845 0.4483745
0.4692747 0.4801248 0.5282953 0.5387154 0.5493255 0.5563656 0.5660457
0.5810758 0.5871859 0.5880459 0.6183762 0.6271763 0.6368964 0.6389064
0.6678067 0.6880269 0.6961170 0.6961970 0.7082871 0.7340373 0.7362074
0.8214782 0.8450485 0.8694387 0.8696087 0.9022290 0.9114191 0.9187892
0.9264793 0.9364694 0.9835098 0.9969800
1011010000000100001100110001001010100010000010010000000011001011001010001
0011010000010100001111110101001001100000000010010000000000101011011000011
0001010000000100000000001000010000000101100101100100111000010000000001000
1011010000100100001100110001001010100010000010010000000011001111001010101
1011010000000100001100110011001010101010000010010000000011001011001010001
0011010000010100001110110101001001100000000010010000000000101011011000011
0000101111001011111100010001101100110000011000011011000100001010101100000
0101010000000100000000001000010000000101100101100100111000010000000001000
1011010000000100001100110011001010101010000010010000000011001011001010001
1011010000100100001100110001001010100010000010010000000011001011001010001
```

Finally, SLiM supports output of samples in VCF format. If the `outputVCFSample()` method is used instead of `outputSample()` in the above recipe, VCF-style output would be produced:

```
##fileformat=VCFv4.2
##fileDate=20160609
##source=SLiM
##INFO=<ID=S,Number=1,Type=Float,Description="Selection Coefficient">
##INFO=<ID=DOM,Number=1,Type=Float,Description="Dominance">
##INFO=<ID=PO,Number=1,Type=Integer,Description="Population of Origin">
##INFO=<ID=GO,Number=1,Type=Integer,Description="Generation of Origin">
##INFO=<ID=MT,Number=1,Type=Integer,Description="Mutation Type">
##INFO=<ID=AC,Number=1,Type=Integer,Description="Allele Count">
##INFO=<ID=DP,Number=1,Type=Integer,Description="Total Depth">
##INFO=<ID=MULTIALLELIC,Number=0,Type=Flag,Description="Multiallelic">
##FORMAT=<ID=GT,Number=1,Type=String,Description="Genotype">
#CHROM  POS  ID  REF  ALT  QUAL  FILTER  INFO  FORMAT  p1:i166  p1:i100
   p1:i462  p1:i8  p1:i0  p1:i314  p1:i318  p1:i488  p1:i81  p1:i287
1  547  .  A  T  1000  PASS  S=0;DOM=0.5;PO=1;GO=4822;MT=1;AC=4;DP=1000
   GT  1|0  0|1  1|0  0|0  0|0  0|0  0|0  0|0  0|0  0|1
1  826  .  A  T  1000  PASS  S=0;DOM=0.5;PO=1;GO=4342;MT=1;AC=5;DP=1000
   GT  0|0  0|0  0|0  1|1  0|1  0|0  1|0  0|0  0|0  1|0
...
```

See sections 20.12.2 and 22.2 for details on these different output methods.

4.2.3 *Sampling individuals rather than genomes*

The previous section showed how to use methods of the `Subpopulation` class to output a sample of genomes from a subpopulation, in either SLiM's own format, or in MS or VCF format. However, in many situations you want to output information about a sample of *individuals*, rather than a sample of genomes – you want to ensure that *pairs* of genomes, each belonging to an individual, are the level of granularity at which the sampling for output occurs. Also, the `Subpopulation` output methods only support sampling from a single subpopulation at a time, but sometimes you want to output a sample drawn from multiple subpopulations, or from the full population. Finally, sometimes you want to output a custom sample that your script chooses itself, rather than a random, equally-weighted sample of the sort that the `Subpopulation` methods allow. These tasks are all quite straightforward using lower-level methods of the `Genome` class. As an illustration of this approach, we will look at a recipe that outputs the genomes of a weighted sample of individuals drawn from the whole population:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "f", 0.01);
    initializeGenomicElementType("g1", c(m1,m2), c(1.0,0.01));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
    sim.addSubpop("p2", 500);
    p1.setMigrationRates(p2, 0.01);
    p2.setMigrationRates(p1, 0.01);
}
10000 late() {
    allIndividuals = sim.subpopulations.individuals;
    w = asFloat(allIndividuals.countOfMutationsOfType(m2) + 1);
    sampledIndividuals = sample(allIndividuals, 10, weights=w);
    sampledIndividuals.genomes.output();
}
```

This model involves a few things that we haven't looked at yet, such as multiple subpopulations connected by migration (see section 5.2.1) and multiple mutation types (see section 7.1). However, those details are not our focus here. For our current purposes, it suffices to recognize that there are two subpopulations, `p1` and `p2`, connected by migration, and there are two mutation types, `m1` and `m2`, with `m1` representing common neutral mutations and `m2` representing less common beneficial mutations. Our focus is on the `late()` event in generation `10000`, which produces the output for the model. We will follow through its logic one line at a time.

The first line defines the set of individuals from which our sample will be drawn, here called `allIndividuals`. The `sim.subpopulations` property gives us a vector of all of the subpopulations in the model (i.e., `p1` and `p2`). The `individuals` property of that vector is then all of the individuals (that is, objects of class `Individual`; see section 21.6) gathered from across those subpopulations.

The second line determines the weights that we will use for sampling, here called `w`. Note that the use of weights here is optional; if you want an unweighted sample, you can skip this line and omit the weights vector in the call to `sample()` below. In this recipe, however, we want the likelihood that an individual is chosen for sampling to be related to the number of `m2` mutations the individual possesses, so we use `countOfMutationsOfType(m2)`. We add `1` to that count, so that individuals with no `m2` mutations have a weight of `1`, individuals with one `m2` mutation have a weight of `2`, and so forth. This is somewhat arbitrary, but it does have the nice property that we are guaranteed that the weights vector is not all zero (which would cause a runtime error, since it would not be possible to draw a sample). If you draw your own samples, you probably want to ensure that the sample can always be drawn, to avoid runtime errors.

The third line draws a sample of `10` individuals from `allIndividuals`, using the `sample()` function and passing it the weights vector `w` (using the named arguments syntax of Eidos, for readability). The sample is put into the temporary variable `sampledIndividuals`.

Finally, the fourth line outputs the genomes of the sampled individuals using the `output()` method of `Genome`. This outputs the sample in SLiM's own format, similarly to what we saw in the previous sections; there are also `outputMS()` and `outputVCF()` methods on `Genome` that can be used similarly to produce MS and VCF output. Since there are two genomes per individual, twenty genomes will be output. Each pair of genomes in the output will come from one sampled individual; in the SLiM and MS output formats this is not explicit, but in the VCF format, since it is a diploid format (as used by SLiM), this pairing into individuals is explicit in the output. See section 21.3.2 for more information on these output methods, and section 23.3 for details on the format of output they generate.

While this recipe implemented one particular sampling scheme, the `Genome` methods used here can be used to output any vector of genomes, whether a random sample or a specifically selected set. The higher-level output methods of `SLiMSim` and `Subpopulation` are a little easier to use, but these low-level methods provide greater power and generality.

4.2.4 Substitutions

The `outputFull()` method of `SLiMSim` does output the full state of the population, but there is some historical state that it does not output. Most notably, it does not output substitutions – mutations which have been fixed and have thus been removed from the population by SLiM for efficiency. If fixed mutations are of interest, SLiM does keep a record of them and can output that record on request. For example, we could output substitutions, in addition to other state, with this script:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
5000 late() { p1.outputSample(10); }
10000 late() { sim.outputFull(); }
10000 late() { sim.outputFixedMutations(); }
```

The only change relative to the previous script is the added line:

```
10000 late() { sim.outputFixedMutations(); }
```

If you copy and paste this script into SLiMgui, Recycle and Play, you will see that at simulation end some additional output appears:

```
#OUT: 10000 F
Mutations:
0 220169 m1 98564 0 0.5 p1 107 1053
1 221802 m1 1217 0 0.5 p1 268 1152
...
```

The header `#OUT: 10000 F` indicates simply that in generation `10000` fixed mutations (`F`) were output. The rest is a list of mutations in almost the same format as before. However, the final number in each line is no longer a prevalence; since the mutation fixed, we know that it was present in every genome in the simulation. Instead, the final number shows the generation number in which the mutation reached fixation. Note that the default behavior of SLiM – that substitutions are removed from all individual genomes – can be deactivated if necessary (see section 21.9.1).

Display of fixed mutations in SLiMgui can also be enabled by clicking the `F` button to the right of the chromosome view; when this display is enabled, fixed mutations will be displayed as full-height bars (blue, by default) in the chromosome view.

4.2.5 Custom output with Eidos

The `outputFull()`, `outputSample()`, `outputMSSample()`, `outputVCFSample()`, and `outputFixedMutations()` methods described in the preceding sections generate output in very fixed formats that may or may not be useful to you. There is one more built-in output method that is described in the reference section – `outputMutations()` – but it, too, may not be what you need. What to do?

This is an area where the power of Eidos really shines, since you can write whatever Eidos script you like to generate whatever kind of output you want. Some of the more advanced recipes in this cookbook will generate custom output of interesting kinds; section 11.1's recipe will include code to calculate and print the F_{ST} between two subpopulations to assess their genetic divergence, for example, and section 13.2's recipe calculates and prints the nucleotide heterozygosity, π, of a population to assess the effects of inbreeding. In this section, we will look at a much simpler example, as an introduction to the topic of custom output using Eidos.

Suppose you are interested only in the base positions of all of the mutations in the population; you can achieve this with the following output event:

```
100 late() { cat(paste(sim.mutations.position, "\n")); }
```

With our basic neutral simulation script, this generates output like:

```
31113
57761
...
```

This is precisely what we want. How does it work? Let's dissect it, step by step, since it is more complex than the Eidos code we've seen so far.

First of all, we have seen the `sim` object before, representing the simulation. This object, which is an Eidos object of class `SLiMSim`, has a property named `mutations` that yields a vector containing all of the mutations in the simulation (a vector of type `object` and class `Mutation`, to be precise). This is the first use we have seen of a *property*; a property is somewhat like a method, in that it is a member of an object, but whereas a method performs an operation (perhaps involving a lot of computation, and perhaps altering the state of the simulation), a property simply corresponds to a value that exists inside the object. The `sim` object knows all of the mutations it contains; it doesn't have to calculate them or create them, it just has to return the value it already has. It is therefore a property – the `mutations` property. The member operator is used to access properties, just as it is used to access methods, so the value of `sim.mutations` is the vector of mutations contained by the simulation.

That value is itself an object. As mentioned before, all values in Eidos are actually vectors; the vector of mutations might contain many elements (each of which is called an *object-element*), but it is nevertheless a single Eidos object. The `Mutation` class in SLiM defines a property, `position`, that is the base position of the mutation; we can access this property on our vector of mutations to get a vector of positions. This involves a certain amount of work behind the scenes; each mutation has its own position, and Eidos must loop over all of the mutations in the vector of mutations, getting the position of each one and pasting all the positions together to make a new vector. Eidos does this for you, though, since Eidos is a vector-based language; so `sim.mutations.position` is all the Eidos code that is needed to get a vector of the positions of all mutations in the simulation.

Peeling the onion back a layer, this expression is contained in a function call:

```
paste(sim.mutations.position, "\n")
```

This function takes a vector argument (`sim.mutations.position`) and pastes all of the elements together to form a single value of type `string`. We haven't really talked about `string` yet; a `string` is simply a sequence of characters, like `"hello, world"`. Eidos can paste strings together, split them apart, and print them out; it can also convert most other types into `string` for the purpose of output. The `paste()` function always produces a `string` as its result; it converts the elements of the vector it is given into `string` elements in order to do so. The second parameter of `paste()`, `"\n"`, is a string containing a single character, the newline character, represented with the escape sequence `\n` (you can read more about strings and escape sequences in the Eidos manual; it is not worth getting into here). The final result is that each of the `integer` positions in `sim.mutations.position` is converted to a string representation and then pasted together with the others, with newlines in between, to produce the desired output as seen above.

Note that this output event is designated as a `late()` event, for the reasons outlined in section 4.2.1; in this case, we wish to see the positions of mutations at the end of generation `100`, not the beginning. With custom output code of this sort, SLiM is not able to infer that it is likely to be an error if it runs in an `early()` event instead, however; so if the `late()` designation is removed here, SLiM will not produce a warning. When writing custom output script events, you need to think carefully about whether they should be `early()` or `late()` events (but a `late()` event is usually what you want).

The simplicity of this example – just a single line of Eidos code! – should make it clear that generating output in whatever format you desire is likely to be straightforward once you get the hang of how Eidos works.

Since the power of this may not be entirely apparent yet, let's consider a problem that might arise in using SLiM. You might wish to produce MS-style output for a sample of genomes spanning the whole population, but the built-in `outputMSSample()` method of `Subpopulation` (sections 4.2.2, 20.12.2, and 22.2.3) only supports generation of MS-style output from a sample of a single subpopulation. As of SLiM 2.1, you can solve this problem with the `outputMS()` method of `Genome` (sections 20.3.2 and 22.3.2), but let's pretend that method doesn't exist; the same general problem will arise whenever you want to output data in a format that SLiM does not, in fact, intrinsically support. Generating MS-style output using Eidos is trivial:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
    sim.addSubpop("p2", 500);
}
```

```
// custom MS-style output from a multi-subpop sample
2000 late() {
    // obtain a random sample of genomes from the whole population
    g = sample(sim.subpopulations.genomes, 10, T);

    // get the unique mutations in the sample, sorted by position
    m = sortBy(unique(g.mutations), "position");

    // print the number of segregating sites
    cat("\n\nsegsites: " + size(m) + "\n");

    // print the positions
    positions = format("%.6f", m.position / sim.chromosome.lastPosition);
    cat("positions: " + paste(positions, " ") + "\n");

    // print the sampled genomes
    for (genome in g)
    {
        hasMuts = (match(m, genome.mutations) >= 0);
        cat(paste(asInteger(hasMuts), "") + "\n");
    }
}
```

This model is quite straightforward; the only complication is that there are two subpopulations, and we wish to produce MS-style output for a sample across both of them. The generation `2000` event does precisely that. First it obtains the genomes upon which the output will be based; here this is done using `sample()` on the vector of all genomes in the simulation, but any other sampling scheme could be used instead. To sample specifically from subpopulations `p1` and `p2`, for example, without sampling from any other subpopulations that might exist, you could do:

```
g = sample(c(p1.genomes, p2.genomes), 10, T);
```

The sample size is `10`, and sampling is done with replacement (the `T` parameter to `sample()`), but that can obviously be customized. Next `unique()` and `sortBy()` are used to get a vector of the mutations present in the sample, sorted by position. The `size()` of that vector is the number of segregating sites, so that is trivial to output. Printing the positions is also simple; `format()` is used to guarantee that every position is formatted with six digits to the right of the decimal, in decimal rather than scientific notation even for very small values. Finally, the sampled genomes are printed in MS format, using `asInteger()` to convert `logical` values from `match()` into `0`s and `1`s.

4.2.6 The simulation endpoint

The astute reader will have noticed that in the previous sections we not only added output events, we also removed one line from the original script:

```
10000 { sim.simulationFinished(); }
```

We can do this because SLiM will generally stop after the last generation in which an event is scheduled. In our basic neutral simulation, however, we had no output commands; if we had omitted the line above with the `simulationFinished()` call the simulation would have ended at the end of generation 1. Alternatively, we could have just written:

```
10000 { }
```

This "empty event" would have caused SLiM to run out to the end of generation `10000`, because there was still a future event scheduled. At the end of generation `10000` SLiM would then stop, since there was no future event after generation `10000` scheduled. In fact, `simulationFinished()`

is really useful only when you wish to end a simulation before it would naturally end on its own. You might check for an equilibrium condition, for example, and end the simulation if it has been at equilibrium for the past `1000` generations, even though it would otherwise have run further.

There is one further caveat to mention regarding how simulations end. It is possible to define an Eidos event that runs in every generation. For example, we could write the following script:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
late() { p1.outputSample(10); }
```

Notice that there is no generation number before the Eidos event defined in the last line; this indicates that the event should be run in every generation, from here to eternity. If you copy and paste this into SLiMgui and Recycle and Play, it will stop at the end of generation `1`, however; there is always a scheduled future event (the output event), but SLiM does not use it in determining when the simulation should end, precisely because it has no expiration date. SLiM assumes that it is not your wish to run a simulation that runs forever – commonly known as an “infinite loop” in programming – so the simulation end is determined without reference to that event.

To define a final generation for the simulation in this situation, you would use precisely the trick described above: just add an “empty event”, like:

```
100 { }
```

The simulation will now run to the end of generation `100`. Note that there is no need to designate the event as a `late()` event; SLiM always runs the last generation to completion, even if `simulationFinished()` is called. The only way to halt a simulation immediately, within a generation, is to call the Eidos error function `stop()`.

5. Demography and population structure

The previous chapter discussed in detail the structure of a basic neutral simulation in SLiM, including `initialize()` callbacks, Eidos events, the `SLiMSim` class, and many of the conceptual underpinnings of SLiM such as mutation types, genomic element types, and chromosome organization. It also covered some basic features of the Eidos language, such as vectors and vector operations, function calls, objects, and method calls. From here, we assume a working knowledge of these topics; you can consult the Eidos manual regarding features of the Eidos language, and the reference section of this manual for details regarding SLiM.

In this chapter, we will focus on building on this foundation to make some simple "recipes" for simulations that do interesting things with demography and population structure.

5.1 Subpopulation size

5.1.1 Instantaneous changes

As we saw in section 4.1.8, we can create a new subpopulation with `sim.addSubpop()`, a method call which takes the initial size of the subpopulation as a parameter. What if we want the population size to change later? This is very straightforward; for example, here is a simple script that models a population that goes through a bottleneck:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 1000); }
1000 { p1.setSubpopulationSize(100); }
2000 { p1.setSubpopulationSize(1000); }
10000 late() { sim.outputFull(); }
```

The `initialize()` callback is unchanged from previous models. In generation `1` a subpopulation named `p1` is set up with an initial size of `1000`. In generation `1000`, a method named `setSubpopulationSize()` is called on `p1` to change its size to `100`, the beginning of the bottleneck. In generation `2000` the size is set back to `1000`, ending the bottleneck. The simulation then executes until it ends in generation `10000` with full output.

If you run this in SLiMgui (don't forget to Recycle), the population size changes as expected.

5.1.2 Exponential growth

Sometimes you may want the size of a subpopulation to vary in a continuous fashion, rather than experiencing discrete changes as in the previous recipe. This is straightforward in SLiM because of the power of Eidos to express mathematical relationships. We will look at several different versions of this recipe in order to explore different aspects of the problem.

As a first example, to make a population experience a period of exponential growth:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
```

```
1 { sim.addSubpop("p1", 100); }
1000:1099 {
    newSize = asInteger(p1.individualCount * 1.03);
    p1.setSubpopulationSize(newSize);
}
10000 late() { sim.outputFull(); }
```

Most of the script is unchanged; the work is done in the second Eidos event, which is scheduled to run from generation `1000` to `1099`, producing exponential growth for `100` generations. This event calculates a new size, assigning it into `newSize`, and then sets the subpopulation size using that variable. The use of the variable is for readability; it would be essentially equivalent to write:

```
p1.setSubpopulationSize(asInteger(p1.individualCount * 1.03));
```

Let's look more closely at that statement. First, the current size of the subpopulation is accessed through the `individualCount` property of `p1`. That size is then multiplied by `1.03` to produce a new size based on an exponential growth rate of `1.03`. Finally, the size is converted to an `integer` by the `asInteger()` function (since `setSubpopulationSize()` does not allow you to set a non-`integer` size), and the `integer` size is passed to `setSubpopulationSize()`. There is a suite of `as...()` functions in Eidos that allow you to convert values to various new types, but converting `float` values to `integer` with `asInteger()` is probably the most common conversion.

An important point here is that the `setSubpopulationSize()` call does not change the current size of the subpopulation; after all, what would the genetics of the new individuals be? Instead, it sets a new target size that will be used the next time that an offspring generation is created; a few additional offspring will be made to reach the new target size. If you access the `individualCount` property immediately after calling `setSubpopulationSize()`, you therefore observe that the individual count has not changed. This is the reason why `setSubpopulationSize()` is not called `setIndividualCount()`; the difference in name is intended to emphasize how SLiM works.

Since the population size gets rounded down to an `integer` in each generation, this code does not actually achieve the precise exponential growth rate of `1.03` that we wanted. Let's fix that:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 100); }
1000:1099 {
    newSize = asInteger(round(1.03^(sim.generation - 999) * 100));
    p1.setSubpopulationSize(newSize);
}
10000 late() { sim.outputFull(); }
```

Running this in SLiMgui shows that the population reaches a size of `1922`, whereas the previous version reached a size of `1630` – a significant difference! Beware accumulated roundoff error.

How does the new version work? The expression `sim.generation-999` computes the number of generations of exponential growth that have occurred; in generation `1000` this is `1`, in generation `1099` it is `100`. Next, `1.03^(sim.generation-999)` raises `1.03` to that power; `^` is the exponentiation operator in Eidos, as in many programming languages. That calculates the result of the exponential growth over the requisite number of generations. Finally, that result is rounded to the nearest whole number by `round()`, which produces a `float` result, and then that whole number is converted to an `integer` by `asInteger()`.

Sometimes we may want the population size to increase exponentially until a specific target size is reached, without knowing how many generations that might take. This is a bit trickier. One possible implementation does this by brute force (leaving out the `initialize()` code):

```
1 { sim.addSubpop("p1", 100); }
1000:2000 {
    if (p1.individualCount < 2000)
    {
       newSize = asInteger(round(1.03^(sim.generation - 999) * 100));
       p1.setSubpopulationSize(newSize);
    }
}
10000 late() { sim.outputFull(); }
```

This uses an `if` statement to increase the size of the subpopulation only if it is still less than `2000` (this is the first time we've seen the `if` statement in Eidos, but it should be pretty obvious what it does here; see the Eidos manual for clarification). The generation range for the event has been expanded to `1000:2000`, because we don't know what generation the target size will be reached in; it will be well before generation `2000`, so this is good enough, but is a bit sloppy. Alternatively, we could calculate the exact generation in which the target size is reached (`1101`, as it happens), and use that instead of `2000`; if we did that, we wouldn't even need the `if` statement, since the exponential growth would reach its target in the event's last invocation.

To ensure that the last generation of growth produces exactly `2000` individuals, we can use the following solution:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 100); }
1000: {
    newSize = round(1.03^(sim.generation - 999) * 100);
    if (newSize > 2000)
       newSize = 2000;
    p1.setSubpopulationSize(asInteger(newSize));
}
10000 late() { sim.outputFull(); }
```

First of all, notice that the generation range for the exponential growth event is now written as `1000:`, omitting the end generation. Just as supplying no generation range at all for an event means "run in every generation", omitting the end generation means "run in every generation after the specified start generation". One may similarly omit the start generation with the syntax `:end`, meaning "run in every generation from the beginning until the specified end generation".

The logic inside the event has also changed. Now the code *always* calculates a new size. If that size is greater than `2000` it gets clamped to `2000`, which enforces the maximum population size we wanted. The clamped size is then set on the subpopulation.

The drawback to this solution is that the event runs in every generation from `1000` onward, calling `setSubpopulationSize()` to set the size to `2000` over and over in generations after the target size has been reached. That is inefficient; more importantly, it might interfere with other changes we might want to make to the population size later in the simulation. We'd really like our event to run for exactly the needed duration to reach the target size, and then not run in subsequent generations, without having to hard-code a final generation for it. There is a simple solution to this problem – and this, you will be relieved to read, is the final, polished version of our exponential growth recipe (so the `initialize()` callback is provided to make the recipe complete):

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 100); }
1000: {
    newSize = asInteger(round(1.03^(sim.generation - 999) * 100));
    if (newSize >= 2000)
    {
       newSize = 2000;
       sim.deregisterScriptBlock(self);
    }
    p1.setSubpopulationSize(newSize);
}
10000 late() { sim.outputFull(); }
```

Braces have been added around the `if` statement's consequent to make a group of statements; all of the statements in the group will be executed if the condition of the `if` statement is true. This use of braces makes what is called a *compound statement*; compound statements are legal anywhere in Eidos that a single statement is legal.

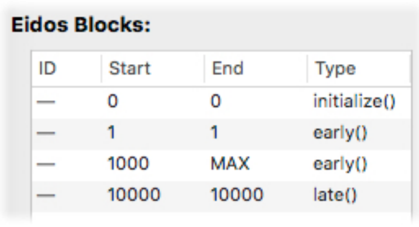
The interesting change here, though, is the addition of the line:

```
sim.deregisterScriptBlock(self);
```

This line prevents the event from continuing to run after the target size has been reached. It is a common pattern in SLiM scripting, so it is worth a bit of discussion. SLiM keeps track of *script blocks* that are registered for execution in the simulation. All of the events and callbacks that you write in your input script are automatically registered; it is also possible to construct and register new script blocks dynamically, as we will see in a later chapter. Script blocks that are registered can be deregistered, using the `deregisterScriptBlock()` method of `SLiMSim`, as we are doing here. Once a block is deregistered, SLiM forgets about it and no longer executes it.

The other thing to be explained here is `self`. This is a variable that is defined whenever SLiM is executing an event or callback; it refers to the currently executing script block. We use it here so that our exponential growth event can deregister itself. Once deregistered, the event is no longer executed, and will remain deregistered until the Recycle button is pressed.

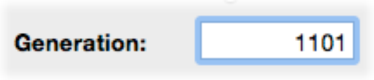
You can see the dynamics of script registration and deregistration graphically in SLiMgui, by the way. Start by pressing Recycle, with the recipe above already pasted into the window. Now if you open the drawer for the simulation window by pressing the drawer button ☞ to the right of the chromosome view area, you will see a list of registered scripts:



Eidos Blocks:

ID	Start	End	Type
—	0	0	initialize()
—	1	1	early()
—	1000	MAX	early()
—	10000	10000	late()

The exponential growth event is listed as the third entry there; if you hover the mouse over its entry for a second or two, you will even see the code for it, shown in a tooltip. Now click in the generation field, enter `1101`, and press return:



This causes SLiMgui to execute the simulation up to the beginning of the requested generation, which is just before the target population size is attained. If you now click Step, you will see the exponential growth event disappear from the list of registered events.

If your scripting gets complicated, with script blocks registering and deregistering frequently, this facility for viewing all of the registered script blocks can prove quite useful.

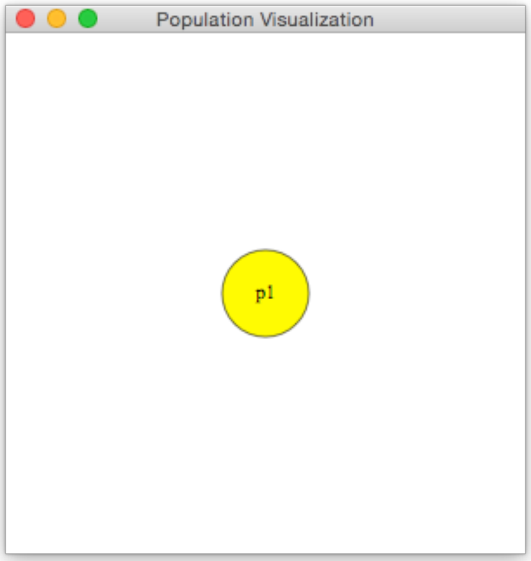
5.1.3 The population visualization graph

In the previous section, we saw several different ways to make a subpopulation grow exponentially for a period of time. In this section, we show how to visualize the dynamics of demography and population structure graphically in SLiMgui on Mac OS X.

Start by copying and pasting the last recipe into a new SLiMgui simulation window, and then Recycle to parse the script and get ready to execute it. Now click on the Show Graph button, , and from its pop-up menu select “Graph Population Visualization”. This will bring up a small window, presently empty.

If you click Step twice, in order to execute the initialization phase and then generation 1, you should see a small yellow circle labeled “p1” appear. This circle represents subpopulation `p1`; in particular, its radius represents the size of the subpopulation, and its color represents the mean fitness value of the subpopulation.

Now press Play, and keep your eyes on the subpopulation circle. When the simulation reaches generation `1000` the circle for `p1` will begin to grow, and it will continue growing until the subpopulation size reaches its target, `2000`:



In this instance the visualization is fairly trivial; still, it is useful for verifying that the population expansion happens in the way that it was planned. In future sections we will see that the population visualization graph can also help us to visualize migration dynamics, fitness dynamics, and other such things, making it a very useful tool for simulation debugging.

5.1.4 *Cyclical changes*

Another common demographic dynamic is a cyclically varying subpopulation size, perhaps representing seasonality, or a decadal oscillation in resource availability. Implementing this in SLiM is quite trivial; for example:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 1500); }
{
    newSize = cos((sim.generation - 1) / 100) * 500 + 1000;
    p1.setSubpopulationSize(asInteger(newSize));
}
10000 late() { sim.outputFull(); }
```

The `initialize()` callback is unchanged. The interesting work is done by the second event – the one with no generation specifier, which you might recall means that it will be executed in every generation. This event first calculates a new size, and then sets the new size in the subpopulation (converting to `integer` as usual). The new size is calculated based upon the current generation, `sim.generation`, passed through the `cos()` function, which calculates a cosine. The generation is scaled and translated in order to arrange that the first offspring generation has a size of `1500`, matching the size of the parental generation set up by `addSubpop()`. Of course that is not required; this particular arrangement is just for demonstration purposes.

The `cos()` function calculates a cosine based on a given angle in radians, as is standard. The periodicity of the cycling is therefore based upon the fact that there are 2π radians in a circle; given the scaling factor of `100`, the population will complete a full cycle in `100*2π` generations, which is about `628`. To make a subpopulation cycle with whatever periodicity you wish, just adjust the scaling factor accordingly. Similarly, since cosine varies between `-1` and `1`, the scaling factor of `500` on that, plus the translation of `1000`, means that the population size cycles between `500` and `1500`. You might wish to view these dynamics in SLiMgui's population visualization graph, as described in the previous section.

This recipe uses `cos()` to generate cyclical dynamics, but you can plug in whatever formula you wish. The population size does not have to depend only upon the generation, either; the flexibility of Eidos allows you to implement whatever demographic model you wish, including demography that depends upon the model dynamics themselves, as we will see in the next section.

5.1.5 *Context-dependent changes: Muller's Ratchet*

Sometimes you might want subpopulation size to depend upon something other than time. An example would be a situation in which population size depends upon mean fitness (e.g., a model of so-called "hard" selection); if the mean fitness is low then the subpopulation size would be small (perhaps because the subpopulation is getting outcompeted by individuals of some other species, or perhaps because the subpopulation is just so unfit that individuals are having trouble surviving and feeding themselves even without competition). Here we will examine such dynamics in a model of Muller's Ratchet:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "e", -0.01);
    m2.convertToSubstitution = F;
    initializeGenomicElementType("g1", c(m1,m2), c(1,1));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 100); }
{
    meanFitness = mean(p1.cachedFitness(NULL));
    newSize = asInteger(100 * meanFitness);
    p1.setSubpopulationSize(newSize);
}
10000 late() { sim.outputFull(); }
```

The `initialize()` callback here has been modified so that there are two mutation types, `m1` and `m2`, produced with equal probability in genomic element type `g1`. The `m1` type represents neutral mutations as usual (a fixed DFE with selection coefficient `0.0`); the `m2` type represents deleterious mutations (an exponential DFE with mean selection coefficient `-0.1`). In our model we want deleterious mutations to continue to affect fitness even after fixation, progressively reducing the population size. For this reason, the `convertToSubstitution` property of `m2` is set to `F` to prevent fixed mutations of that type from being replaced by `Substitution` objects (see sections 18.3 and 20.9.1 for further information on this property).

The `cachedFitness()` method of class `Subpopulation`, called on `p1`, provides a vector of the fitness values of all individuals in the subpopulation (a vector of indices could be passed, to request fitness values only for specified individuals; the `NULL` value passed simply requests fitness values for all individuals). The `mean()` function calculated the arithmetic mean of the vector it is passed, resulting in the mean subpopulation fitness. A new size for the subpopulation is then calculated using a base size of `100`, representing the size if the population were of mean fitness `1.0`. In our scenario, the base size is simply multiplied by the mean fitness, but one can of course use any other function for this.

This recipe is a very primitive toy model of fitness-based population dynamics; nevertheless, it is interesting to look at it in the population visualization graph, where the population size changes visibly and is clearly correlated with mean fitness, shown as the color of the subpopulation. As deleterious mutations accumulate in the subpopulation, its circle both reddens and shrinks, showing visually that demography is being driven by mean fitness. When the subpopulation reaches extinction due to the accumulation of deleterious mutations by Muller's Ratchet, this model terminates with an error ("undefined identifier p1"), because after subpopulation `p1` is set to a size of `0` the symbol `p1` ceases to exist; setting a size of `0` tells SLiM to remove the subpopulation entirely. One could end the simulation more gracefully by testing for `(newSize == 0)` and calling `sim.simulationTerminated()`, perhaps after producing some sort of output regarding the generation and the number of deleterious mutations fixed.

5.2 Population structure

5.2.1 Adding subpopulations

We have already seen in previous recipes how to add a single subpopulation by calling the `addSubpop()` method of `sim` (which is of class `SLiMSim`). Creating population structure by adding multiple subpopulations – of different sizes, linked by migration – is a very simple extension of that:

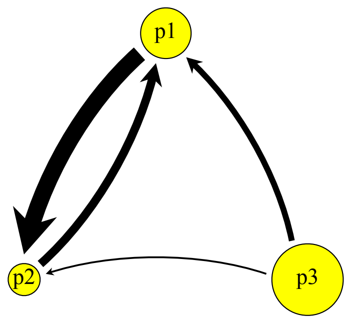
```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
    sim.addSubpop("p2", 100);
    sim.addSubpop("p3", 1000);
    p1.setMigrationRates(c(p2,p3), c(0.2,0.1));
    p2.setMigrationRates(c(p1,p3), c(0.8,0.01));
}
10000 late() { sim.outputFull(); }
```

For this recipe we have returned to the simple `initialize()` callback we started with, with only one mutation type. The new action happens in the generation `1` event, where we now add three subpopulations of different sizes. Those populations are then connected by migration using calls to the `setMigrationRates()` method of `Subpopulation`. Let's examine the first such call:

```
p1.setMigrationRates(c(p2,p3), c(0.2,0.1));
```

Since this method call is made on `p1`, it is setting the *immigration into* `p1`. Both `p2` and `p3` are given as sources of immigration, with rates of `0.2` and `0.1` respectively. In SLiM's design, this does not mean that individuals from `p2` and `p3` will move from those populations into `p1`. Rather, it means that when p1 generates an offspring generation, and parents are chosen for a new offspring individual, a proportion of `0.2` of those parents will be chosen from `p2`, a proportion of `0.1` from `p3`, and the remaining proportion of `0.7` will be chosen from `p1` itself, since the default behavior is that parents are chosen from the subpopulation into which the new offspring will be placed. The next line sets up migration into p2, in the same way. Since migration into p3 is not configured, p3 acts as a source only. Note that, as discussed further in section 19.2.1, migration rates specify the probability that any given offspring individual will come from a particular source subpopulation; the actual number of migrants in a given generation is thus stochastic, not deterministic.

It can be hard to visualize complex population structure just from code like this; happily, SLiMgui's population visualization graph provides a nice way to see what's going on. If you copy and paste the above recipe into a simulation window, Recycle, press Step twice so that generation 1 has been executed, and then open the population visualization graph, you will see a nice graphical representation of the population structure:



As before, the size of the circle for a subpopulation represents the subpopulation's size, and the color of the circle indicates the mean fitness of that subpopulation. The arrows show migration links, with the thicknesses of the arrows indicating the strength of each link. Here it is immediately obvious that p3 is a source, and that p2 is somewhat close to being a sink but does contribute some immigrants to p1.

Of course there is no need for the population structure to all be set up in generation 1; you can add subpopulations, remove subpopulations, and change migration rates in each generation if you wish, as we will explore in the next section. The population visualization graph will update to show the current population structure as your simulation runs.

5.2.2 Removing subpopulations

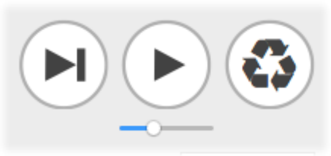
The population structure set up in the previous recipe was quite static, established in generation 1 and unchanging subsequently. Let's explore more dynamic population structure by both adding and removing subpopulations over time and dynamically changing migration. The recipe here is longer because it does more things, but it is only a small extension of previous concepts:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
100 { sim.addSubpop("p2", 100); }
100:150 {
    migrationProgress = (sim.generation - 100) / 50;
    p1.setMigrationRates(p2, 0.2 * migrationProgress);
    p2.setMigrationRates(p1, 0.8 * migrationProgress);
}
1000 { sim.addSubpop("p3", 10); }
1000:1100 {
    p3Progress = (sim.generation - 1000) / 100;
    p3.setSubpopulationSize(asInteger(990 * p3Progress + 10));
    p1.setMigrationRates(p3, 0.1 * p3Progress);
    p2.setMigrationRates(p3, 0.01 * p3Progress);
}
2000 { p2.setSubpopulationSize(0); }
10000 late() { sim.outputFull(); }
```

The initialize() callback is as before. Subpopulations p1, p2, and p3 are now set up in generations 1, 100, and 1000 respectively. Subpopulation p2 is removed in generation 2000 by setting its size to 0; that is all that is needed to remove a subpopulation.

The rest of the code – the 100:150 event and the 1000:1100 event – introduces some continuous change into the population structure. In the 100:150 event the migration rates between p1 and the newly established p2 grow over time until they reach a target rate. In the 1000:1100 event the new subpopulation p3 grows in size over time, from a very small founder population, and its migrational contribution to p1 and p2 grows over time as p3 grows in size.

Watching these dynamics in SLiMgui's population visualization graph is useful for confirming that they are functioning correctly. However, the simulation may go too fast for the dynamics to be seen clearly. You can use the speed slider, directly below the Play button, to slow it down:



If you set a slower speed, as above, and then Recycle and Play, it should be easier to follow the action.

5.2.3 Splitting subpopulations

By default, when new subpopulations are added in SLiM they are composed of "brand-new" individuals with no mutations. To produce more realistic dynamics, we might like the new subpopulations to be split off from an existing subpopulation. Modifying the recipe above, this is quite a simple change:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
100 { sim.addSubpopSplit("p2", 100, p1); }
100:150 {
    migrationProgress = (sim.generation - 100) / 50;
    p1.setMigrationRates(p2, 0.2 * migrationProgress);
    p2.setMigrationRates(p1, 0.8 * migrationProgress);
}
1000 { sim.addSubpopSplit("p3", 10, p2); }
1000:1100 {
    p3Progress = (sim.generation - 1000) / 100;
    p3.setSubpopulationSize(asInteger(990 * p3Progress + 10));
    p1.setMigrationRates(p3, 0.1 * p3Progress);
    p2.setMigrationRates(p3, 0.01 * p3Progress);
}
2000 { p2.setSubpopulationSize(0); }
10000 late() { sim.outputFull(); }
```

The only change is that the `addSubpop()` calls that established `p2` and `p3` have been changed to `addSubpopSplit()`. This call is very similar to `addSubpop()`, but takes an extra parameter: the existing subpopulation from which the new subpopulation should be split. The split is accomplished by copying the individuals for the new subpopulation from the source subpopulation. In other words, each new individual is an exact genetic clone of an existing individual in the source population, mimicking a founding event in which a subset of the individuals in the source subpopulation find themselves split off into founders of a new subpopulation. (From this perspective it is a bit odd that the founders also remain in the source subpopulation, admittedly, but this is unlikely to be important to simulation dynamics in realistic scenarios since source subpopulations are typically large and founding subpopulations are typically small.)

5.3 Migration and admixture

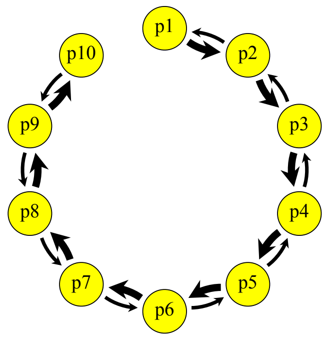
The previous subsections already showed how to set up patterns of migration among multiple subpopulations. Here, we will focus on recipes for a few standard types of population structure to show how the flexibility of Eidos makes setting up complex population structure easy.

5.3.1 A linear island model

This model describes a linear chain of subpopulations, each of which is connected by migration only to its nearest neighbors. This is quite easy to set up:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    subpopCount = 10;
    for (i in 1:subpopCount)
       sim.addSubpop(i, 500);
    for (i in 2:subpopCount)
       sim.subpopulations[i-1].setMigrationRates(i-1, 0.2);
    for (i in 1:(subpopCount-1))
       sim.subpopulations[i-1].setMigrationRates(i+1, 0.05);
}
10000 late() { sim.outputFull(); }
```

If you copy and paste this into SLiMgui, Recycle, do Step twice to step through generation 1, and open the population visualization graph, you will see the resulting structure:



As you can see, migration is stronger in one direction than in the other; this might represent gene flow in a river system, for example, where gene flow is more likely to go downstream than upstream. Indeed, it would be trivial to interrupt the upstream gene flow completely in certain spots to represent the effect of waterfalls that prevent upstream migration. Using the techniques shown in previous sections, it would also be trivial to make the migration pattern change over time; a major flooding event in one generation could allow gene flow to pass upstream past a small waterfall, for example.

This population structure is achieved using three `for` loops. We saw `for` loops briefly in section 4.1.5; let's revisit the concept now. The first loop in this recipe is:

```
for (i in 1:subpopCount)
    sim.addSubpop(i, 500);
```

This causes the statement `sim.addSubpop(i, 500);` to be executed repeatedly as the loop index variable `i` varies from `1` up to `subpopCount`, following the sequence defined by `1:subpopCount`. The result is that new subpopulations are created in order: `p1`, `p2`, `p3`, and on up to `subpopCount`.

The second loop is almost as straightforward:

```
for (i in 2:subpopCount)
    sim.subpopulations[i-1].setMigrationRates(i-1, 0.2);
```

This sets up migration into each subpopulation from the previous subpopulation: into `p2` from `p1`, into `p3` from `p2`, and so forth. Since `p1` receives no such migration (there being no `p0` subpopulation), the loop starts at `2`, not `1`. For each value of `i`, the corresponding subpopulation is looked up in the simulations subpopulation array, which is a property of `SLiMSim`, using `sim.subpopulations[i-1]`; the use of `i-1` here instead of `i` is because `p1` will be at index `0` in the subpopulation array (since vectors in Eidos are numbered starting at `0`, not `1`). Given the proper subpopulation, the `setMigrationRates()` call then sets up migration from the previous subpopulation (which is the purpose of `i-1` in that call).

Given that explanation, the operation of the third loop should be fairly obvious. The power of this algorithmic approach to setting up population structure should be clear; if we want `1000` subpopulations arranged in this manner, all we have to do is change `subpopCount = 10;` to `subpopCount = 1000;`. The population visualization graph in SLiMgui will find this a bit challenging to display, but it should be possible to test and debug such a model with just `10` subpopulations, and then scale up to `1000` subpopulations for your production runs.

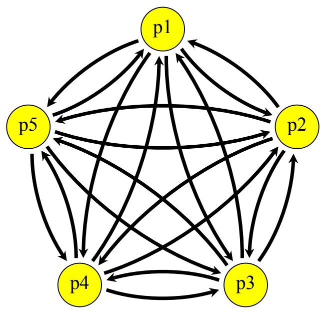
5.3.2 A non-spatial metapopulation

Another possible scenario is a non-spatial metapopulation in which migration between each pair of subpopulations occurs at some constant rate. This can be set up as follows:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    subpopCount = 5;
    for (i in 1:subpopCount)
       sim.addSubpop(i, 500);
    for (i in 1:subpopCount)
       for (j in 1:subpopCount)
          if (i != j)
             sim.subpopulations[i-1].setMigrationRates(j, 0.05);
}
10000 late() { sim.outputFull(); }
```

Here a nested pair of `for` loops using index variables `i` and `j` sets up the migration from `j` into `i` for each pair of subpopulations. The test `if (i!=j)` prevents the code from attempting to set the migration rate from a subpopulation into itself, which is illegal.

SLiMgui's visualization of this population structure looks like what we wanted:



This recipe uses only five subpopulations (`subpopCount = 5`), but again the code is general and may be scaled up to however many subpopulations you want in your metapopulation (although SLiMgui may not be very good at visualizing these scenarios once they become too complex).

5.3.3 A two-dimensional subpopulation matrix

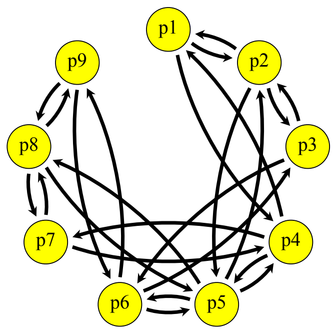
A third common population structure is a two-dimensional grid or matrix of subpopulations, representing a spatial metapopulation in which each subpopulation exchanges migrants only with its direct neighbors. SLiM has no intrinsic concept of geographic space in its simulations, but with a population structure like this a pseudo-geographic regime can be imposed upon a SLiM simulation such that new beneficial mutations, for example, will spread from subpopulation to subpopulation in a similar manner to how they might spread across a real landscape.

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    metapopSide = 3;   // number of subpops along one side of the grid
    metapopSize = metapopSide * metapopSide;
    for (i in 1:metapopSize)
       sim.addSubpop(i, 500);

    subpops = sim.subpopulations;
    for (x in 1:metapopSide)
       for (y in 1:metapopSide)
       {
          destID = (x - 1) + (y - 1) * metapopSide + 1;
          destSubpop = subpops[destID - 1];
          if (x > 1)   // left to right
             destSubpop.setMigrationRates(destID - 1, 0.05);
          if (x < metapopSide)   // right to left
             destSubpop.setMigrationRates(destID + 1, 0.05);
          if (y > 1)   // top to bottom
             destSubpop.setMigrationRates(destID - metapopSide, 0.05);
          if (y < metapopSide)   // bottom to top
             destSubpop.setMigrationRates(destID + metapopSide, 0.05);
       }
}
10000 late() { sim.outputFull(); }
```

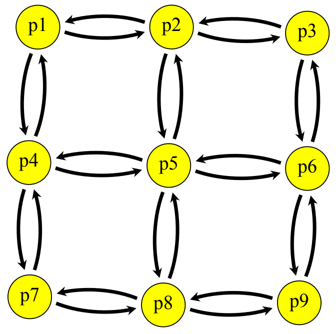
This code is a bit more complex than previous recipes. In the generation `1` event, we first decide how large of a metapopulation we want; `metapopSide=3` means that we will make a 3x3 metapopulation (trivially small, but easier to check for correctness). This can be scaled up arbitrarily; it works well in SLiMgui for values as large as a 1000x1000 metapopulation with 10 individuals per subpopulation. We calculate the number of subpopulations we will need, and make them all with the first `for` loop.

Then comes the trickier part. We loop over the grid of subpopulations using `x` and `y`, which each range from `1` to `metapopSide`. For each subpopulation in the grid, as determined by `x` and `y`, we calculate the ID of the subpopulation in `destID`, and then fetch the subpopulation itself into `destSubpop`, getting it from the simulation's subpopulation array as before. We then set the migration into `destSubpop` from each of its four sides; if it is at the edge of the matrix, it receives no migrants from that side (although it would be trivial to modify this code to make a wrap-around pattern of migration simulating a toroidal world). Simple arithmetic is used to determine the identifier of neighboring subpopulations based upon `destID`.

SLiMgui's visualization of this setup is complicated; it is not immediately obvious that it represents a two-dimensional metapopulation, but it does:



However, SLiMgui has an alternate method of display for these population visualizations. If you control-click or right-click on the graph, you will get a pop-up menu. Select "Optimized Positions" from that menu, and you should see something more like this:



Here it is much more obvious that the migration pattern is as desired. This positioning optimization algorithm is based on a concept called force-directed layout. It is a somewhat experimental feature in SLiMgui, and may not always give layouts that look good; it is also quite slow for layouts involving more than a dozen or so subpopulations. However, it is worth a try if you want to get a publication-worthy picture of your population structure.

Speaking of "publication-worthy", note that when you control-click or right-click on the visualization graph, the pop-up menu also has an item entitled "Copy Graph". That copies the graph to the clipboard as a PDF – very handy for pasting into documents or slides.

5.3.4 A random, sparse spatial metapopulation

The recipe in section 5.3.3 showed how to make a small spatial metapopulation in which subpopulations are arranged spatially in a grid that is connected by orthogonal migration. Here we will extend that recipe to a larger size and a more random metapopulation configuration, and we'll look at a very simple sweep of a beneficial mutation across the metapopulation.

The `initialize()` callback for this model is largely unchanged from section 5.3.3:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "f", 0.3);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
```

The only modification here is the addition of a new mutation type, `m2`, which has been defined to represent beneficial mutations (with a selection coefficient of `0.3`). New mutations are still always neutral (mutation type `m1`); we will introduce the sweep mutation ourselves in script.

The final output event is also unchanged:

```
10000 late() { sim.outputFull(); }
```

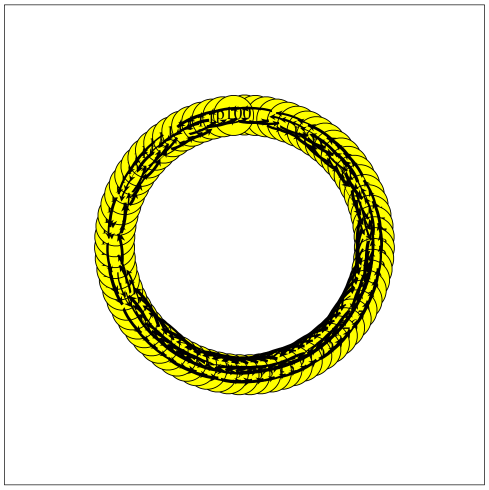
The interesting changes are to the `1 late()` event that configures the initial state of the metapopulation:

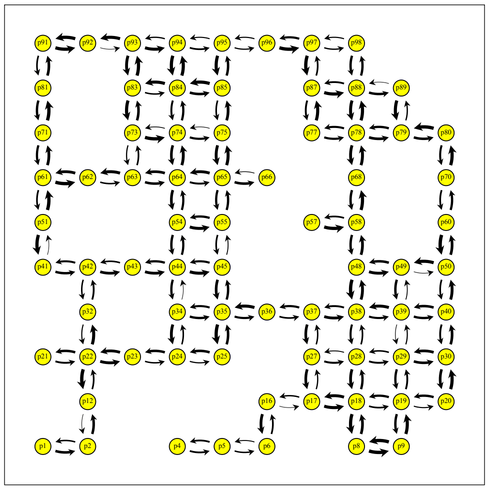
```
1 late() {
    mSide = 10;   // number of subpops along one side of the grid
    for (i in 1:(mSide * mSide))
       sim.addSubpop(i, 500);

    subpops = sim.subpopulations;
    for (x in 1:mSide)
       for (y in 1:mSide)
       {
          destID = (x - 1) + (y - 1) * mSide + 1;
          ds = subpops[destID - 1];
          if (x > 1)   // left to right
             ds.setMigrationRates(destID - 1, runif(1, 0.0, 0.05));
          if (x < mSide)   // right to left
             ds.setMigrationRates(destID + 1, runif(1, 0.0, 0.05));
          if (y > 1)   // top to bottom
             ds.setMigrationRates(destID - mSide, runif(1, 0.0, 0.05));
          if (y < mSide)   // bottom to top
             ds.setMigrationRates(destID + mSide, runif(1, 0.0, 0.05));

          // set up SLiMgui's population visualization nicely
          xd = ((x - 1) / (mSide - 1)) * 0.9 + 0.05;
          yd = ((y - 1) / (mSide - 1)) * 0.9 + 0.05;
          ds.configureDisplay(c(xd, yd), 0.4);
       }

    // remove 25% of the subpopulations
    subpops[sample(0:99, 25)].setSubpopulationSize(0);

    // introduce a beneficial mutation
    target_subpop = sample(sim.subpopulations, 1);
    sample(target_subpop.genomes, 10).addNewDrawnMutation(m2, 20000);
}
```

This creates a 10×10 spatial metapopulation in much the same way as section 5.3.3 created a 3×3 metapopulation: first by creating the subpopulations themselves in a simple loop, and then setting up the migration among them with a pair of nested loops over `x` and `y` (see section 5.3.3 for further comments on that basic design).

For each subpopulation, however, it also does something new, under the `// set up SLiMgui` comment: it calculates a visual position for the subpopulation, as `xd` and `yd`, and then calls `configureDisplay()` on the subpopulation to tell SLiMgui to use that position in its display. The coordinate system used by SLiMgui for subpopulation display spans [0,1] in *x* and *y*, so the `xd` and `yd` values calculated here are within that range. We pass a value of `0.4` for the second parameter to `configureDisplay()`; this is a scaling factor for the circle used to represent the subpopulation, so here we are telling SLiMgui to use unusually small circles (so that all 100 subpopulations fit into the display without overlapping).

If we ran the model *without* this display configuration (just comment out the call to `configureDisplay()`, we would get the left-hand plot; the subpopulations are all overlapping and nothing can be discerned at all. (The "Optimized Positions" technique shown in section 5.3.3 is not up to the task either; optimizing such a large network is a difficult problem. Perhaps that experimental feature will eventually be improved to the point that it produces acceptable results for this model, but at present it does not.) If we run it *with* the display configuration, we get the right-hand plot, which is obviously much better:





Looking at the right-hand visualization, it is now immediately apparent that this is not a complete metapopulation, but rather a sparse metapopulation in which some subpopulations are missing. That brings us to the next lines in the event:

```
// remove 25% of the subpopulations
subpops[sample(0:99, 25)].setSubpopulationSize(0);
```

This takes a sample, of size `25`, from the sequence `0:99`, selects those subpopulations (using the subset operator on `subpops`), and sets their size to zero. As we saw in section 5.2.2, this removes those subpopulations from the simulation; any connections they have to other subpopulations by migration are broken. That one line, then, very easily produces a random sparse metapopulation. The only caveat is that, depending upon which subpopulations get removed, the remaining metapopulation might not be connected; there might be two or more isolated networks with no connection between them via migration at all. If that is undesirable, further steps would have to be taken to avoid the possibility.

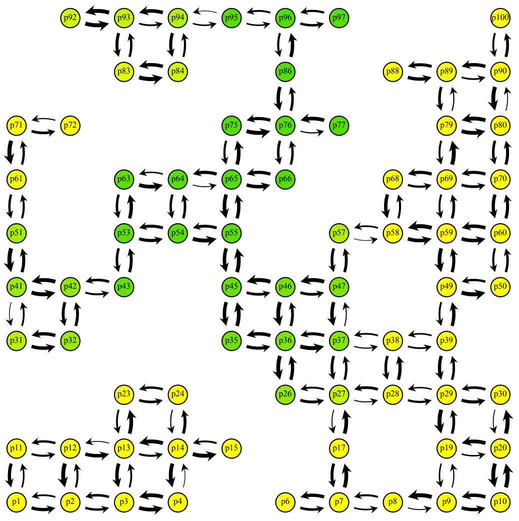
You might also notice that the arrows in the population visualization now vary in their thickness; this is because we now draw random migration rates using `runif()`, rather than using a fixed migration rate as we did in section 5.3.3. This code draws migration rates from a uniform distribution, and makes no attempt to ensure that migration rates between a given pair of subpopulations are symmetric; since this is just scripting, one could implement any pattern of random migration one wished.

That brings us to the final lines of the event:

```
// introduce a beneficial mutation
target_subpop = sample(sim.subpopulations, 1);
sample(target_subpop.genomes, 10).addNewDrawnMutation(m2, 20000);
```

This manual will cover introduced mutations and selective sweeps in great detail in chapter 10, so this is just a tiny bit of foreshadowing of that complex topic. The idea here is simple: we choose one subpopulation from the subpopulations that remain in the model using `sample()`, and then we choose ten genomes at random from the chosen subpopulation again using `sample()` (starting with ten rather than just one to make it more likely that the mutation will not be lost due to drift early on, for pedagogical purposes), and finally we call `addNewDrawnMutation()` to add a new `m2` mutation to those ten genomes at position `20000`. This code, then, introduces a beneficial mutation that will, we hope, sweep through our sparse metapopulation.

And if it doesn't get lost, and if the metapopulation is connected, sweep it does. Here is a screenshot from midway through the sweep:



As per the default behavior in SLiM, subpopulations are colored according to their mean fitness; populations where the sweep mutation is approaching fixation are thus a dark green, while populations that are still neutral are still yellow. Note that the `configureDisplay()` method has a third (optional) argument that would allow us to customize the color of each subpopulation as well, coloring them according to whatever model variable we wish; we have not used that here, since the default fitness-based coloring is in fact exactly what we want.

5.3.5 Reading a migration matrix from a file

Sometimes, when modeling an empirical population, migration rates are specified in a file, and you would like to read that file in and create a corresponding SLiM model. This is very easy to accomplish using Eidos in SLiM. Let's start by looking at a very simple migration matrix file:

```
// For the recipe of section 5.3.4.
// Format: <src>, <dest>, <rate>.
1,1,0.78
1,2,0.10
1,3,0.12
2,1,0.01
2,2,0.96
2,3,0.03
3,1,0.33
3,2,0.17
3,3,0.50
```

This file expresses the model's migration rates as a series of lines, each of which is a series of comma-separated values; this format is often called a CSV file. Let us suppose that it exists on disk at the path `~/Desktop/migration.csv`. The first two lines are comments, describing the file. The rest of the lines each have three values: the identifier of the source subpopulation, the identifier of the destination subpopulation, and the migration rate (sometimes the destination is listed before the source in these sorts of files, so be careful). Note that there are lines expressing the fraction of each subpopulation that does *not* migrate – the remainder after all migrants have left. This is not optimal for SLiM's purposes, but we want to work with the file as it is.

We can read this file in and create a model based on it with a simple script:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    for (i in 1:3)
       sim.addSubpop(i, 1000);
    subpops = sim.subpopulations;

    lines = readFile("~/Desktop/migration.csv");
    lines = lines[substr(lines, 0, 1) != "//"];

    for (line in lines)
    {
       fields = strsplit(line, ",");
       i = asInteger(fields[0]);
       j = asInteger(fields[1]);
       m = asFloat(fields[2]);

       if (i != j)
       {
          p_i = subpops[subpops.id == i];
          p_j = subpops[subpops.id == j];
          p_j.setMigrationRates(p_i, m);
       }
    }
}
10000 late() { sim.outputFull(); }
```

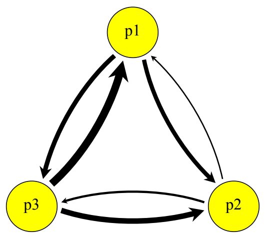
The generation `1` event is where the action is. It first creates the three subpopulations of the model with a simple `for` loop. It would be simple to extend this model to determine the number of subpopulations from the contents of the `migration.csv` file, and to read subpopulation sizes in from that file, and so forth. Here, however, we hard-code those values for simplicity. Once the subpopulations have been created, we cache the vector of subpopulations in `subpops` for brevity in the script that follows.

Next, the script reads in the contents of the `migration.csv` file using `readFile()`. This creates a `string` vector, with each line of the file being a separate element in the vector. The following line uses the `substr()` function to find lines that begin with `"//"`, and removes those lines by subsetting the `lines` vector, stripping out the comment lines from the file.

Now we can loop through the lines with a for loop and handle each line in turn. The `strsplit()` function is used to split `line` into its components, separated by commas; this is often a very convenient way to parse CSV files. The three values of the line are then extracted from the `fields` vector, which is of type `string`, and are converted to their appropriate types.

The last block actually sets the migration rate. First it checks that `i` and `j` are not the same; this filters away the lines that express the non-migrating fractions, which SLiM does not need to know about. Then it looks up the subpopulations referenced by `i` and `j`, using the `id` property, which corresponds to the numeric part of the subpopulation's symbol (i.e., subpopulation `p3` has an id of `3`). Finally, it sets the migration rate from `p_j` to `p_i` to be the rate `m` that was read from the file.

When executed, SLiMgui's visualization of this population structure looks like this:



That looks like what we would expect from looking at the file; `p2` is a sink, `p3` is a source, and `p1` is close to balanced. This is a very simple population model, but this script could just as easily read in a migration matrix file for hundreds or even thousands of subpopulations; its code is in quite general. As mentioned above, it could easily be extended to read subpopulation sizes from the CSV file as well; indeed, other subpopulation properties, such as selfing rates and sex ratios, could also easily be added to the file format and set up by this script, and the script could easily be adapted to work with whatever empirical data files already exist.

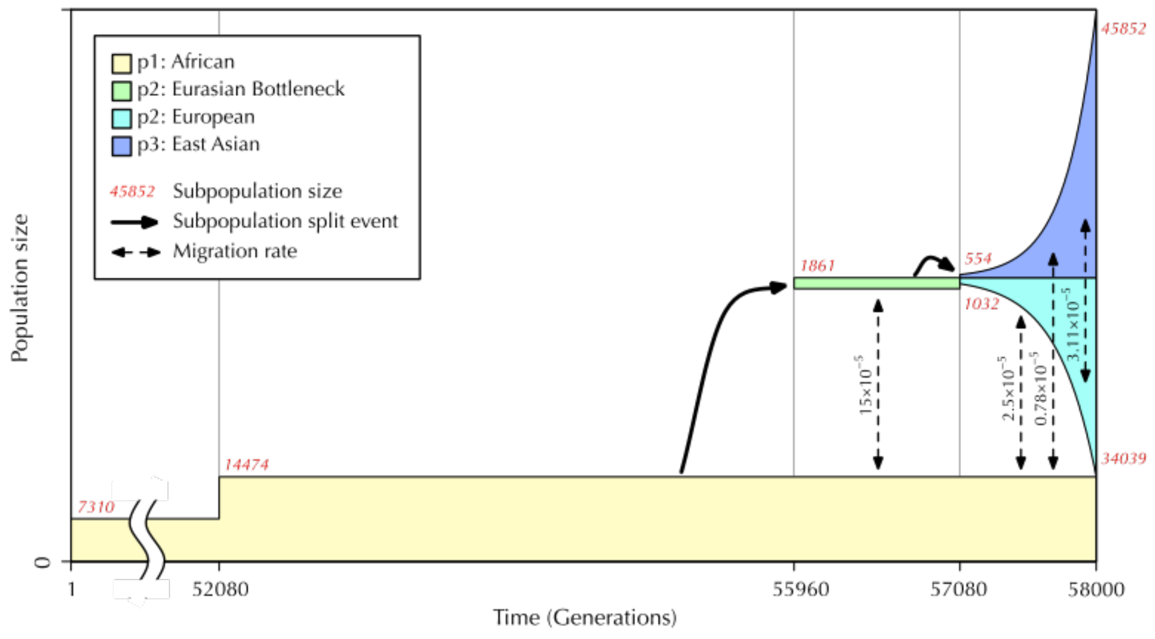
5.4 The Gravel et al. (2011) model of human evolution

In this section we will look at a recipe that brings together all of the elements of demography and population structure that have been discussed in this chapter. This is a SLiM implementation of a model of human evolution presented by Gravel et al. (2011); in particular, we here model the "Low-coverage + exons" model described in their Table 2. The recipe:

```
initialize() {
    initializeMutationRate(2.36e-8);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 10000);
    initializeRecombinationRate(1e-8);
}

// Create the ancestral African population
1 { sim.addSubpop("p1", 7310); }

// Expand the African population to 14474
// This occurs 148000 years (5920) generations ago
52080 { p1.setSubpopulationSize(14474); }

// Split non-Africans from Africans and set up migration between them
// This occurs 51000 years (2040 generations) ago
55960 {
    sim.addSubpopSplit("p2", 1861, p1);
    p1.setMigrationRates(c(p2), c(15e-5));
    p2.setMigrationRates(c(p1), c(15e-5));
}
```

```
// Split p2 into European and East Asian subpopulations
// This occurs 23000 years (920 generations) ago
57080 {
    sim.addSubpopSplit("p3", 554, p2);
    p2.setSubpopulationSize(1032);  // reduce European size

    // Set migration rates for the rest of the simulation
    p1.setMigrationRates(c(p2, p3), c(2.5e-5, 0.78e-5));
    p2.setMigrationRates(c(p1, p3), c(2.5e-5, 3.11e-5));
    p3.setMigrationRates(c(p1, p2), c(0.78e-5, 3.11e-5));
}

// Set up exponential growth in Europe and East Asia
// Where N(0) is the base subpopulation size and t = gen - 57080:
//    N(Europe) should be int(round(N(0) * e^(0.0038*t)))
//    N(East Asia) should be int(round(N(0) * e^(0.0048*t)))
57080:58000 {
    t = sim.generation - 57080;
    p2_size = round(1032 * exp(0.0038 * t));
    p3_size = round(554 * exp(0.0048 * t));

    p2.setSubpopulationSize(asInteger(p2_size));
    p3.setSubpopulationSize(asInteger(p3_size));
}

// Generation 58000 is the present.  Output and terminate.
58000 late() {
    p1.outputSample(216); // YRI phase 3 sample of size 108
    p2.outputSample(198); // CEU phase 3 sample of size 99
    p3.outputSample(206); // CHB phase 3 sample of size 103
}
```

Three subpopulations are modeled in this recipe, as shown in the diagram below (solid arrows showing subpopulation splitting events, dotted arrows showing migration rates between subpopulations, and red italic numbers showing subpopulation effective sizes).



The first subpopulation, present from the beginning of the simulation, is `p1`; it represents Africans (YRI). The second, `p2`, initially represents the Ancestral Eurasian Bottleneck, and then becomes the Europeans (CEU). The third, `p3`, represents East Asians (CHB). As you can see in the diagram and in the recipe above, `p2` splits from `p1` at generation `55960`, and then `p3` splits off from `p2` at generation `57080`. Beginning with the split of `p3` from `p2`, both `p2` and `p3` undergo exponential growth until the end of the model.

The model begins `58000` generations ago (1.45 million years if we assume 25 years per generation). It spends quite a long time doing neutral burn-in before the action really starts in generation `52080` with the expansion of the African subpopulation. Running the full model only takes a couple of minutes, but if you're impatient, you can decrease the generation ranges for all events by `52000`, providing an `80`-generation burn-in that should suffice for illustrative purposes (but will not produce the correct pattern of neutral diversity at the end of the run).

This model is a neutral model; the only mutation type modeled is `m1`, which represents neutral mutations. At the end of the model, random samples are output from each of the three subpopulations to provide a view on the neutral diversity present in each subpopulation. The empirical samples that this output is intended to match were taken from (diploid) humans; the `outputSample()` method of `Subpopulation`, on the other hand, takes as its argument the number of (haploid) genomes to sample and output. The sample sizes in SLiM are therefore double the number of humans sampled empirically.

It is worth noting that the population sizes used in this model are effective population sizes. The actual population sizes in human history were likely much larger, but geography and other factors greatly reduced the effective population size. This is also the reason that the sizes of `p2` and `p3` post-split are not modeled as adding up to the same size as the pre-split `p2` subpopulation.

The model for this recipe was written by Aaron Sams of the Messer Lab at Cornell.

5.5 Rescaling population sizes to improve simulation performance

The limiting factor in most forward population genetic simulations tends to be the actual number of individuals simulated. In SLiM, every individual in the population is modeled explicitly. Thus, in larger populations more time is consumed per generation creating the children that make up the population, and more memory is needed for storing their genetic information.

Perhaps we can approximate the evolution of a large population using simulation of a smaller population? In some ways, we can: analytical theory predicts that under certain assumptions many important population genetic parameters, such as the expected levels of diversity, polymorphism frequency spectra, levels of linkage disequilibrium, etc., should primarily depend on products of the form $N\mu$, Nr, and Ns, where N is the effective population size, μ is the mutation rate, r the recombination rate, and s the selection coefficient of a given mutation.

Thus, for many analyses we do not have to simulate a population of the true size, but can obtain similar results by simulating a much smaller population while rescaling μ, r, and s such that the products $N\mu$, Nr, and Ns remain the same. Importantly, when rescaling population sizes, time has to be rescaled as well, because drift will be faster in a smaller population. The amount of drift in a Wright-Fisher population of 1000 individuals, observed over 100 generations, will be similar to that in a population of 100 individuals observed over just 10 generations. In this way, rescaling a simulation to a smaller population size not only helps us by having to model fewer individuals per generation, but also by reducing the number of generations we need to simulate.

This rescaling "trick" can be tremendously helpful in practice, allowing the simulation of scenarios featuring large populations that would not be feasible to simulate when using their actual population sizes. However, there are clear limitations to rescaling as well. Most obviously, there will be limits to how far downscaling of population sizes can be pushed in the light of an increasing impact of discretization effects: as simulated population sizes become smaller, there will be fewer possible population frequencies at which mutations can segregate, with the lowest possible frequency being 1/(2*N*). Thus, the rescaling approach will break down if the goal is to study the characteristics of very low-frequency polymorphisms.

The discreteness of generations can increasingly become a problem as time is rescaled downwards. For example, if a selective sweep that takes 100 generations in a population of 10000 individuals takes the same amount of "time" in a downscaled population of 500 individuals, it would complete in only 5 generations (assuming selection coefficients were rescaled upwards accordingly). In that case, the frequency changes of the selected allele will no longer be small over the timescale of a single generation, violating a key assumption in many analytical models. Furthermore, since the time for a beneficial allele to sweep scales with log(*N*), we actually expect the sweep in the smaller population to complete even *faster* than we would expect after accounting for rescaling.

This discretization can also have unexpected and undesirable side effects on processes such as adaptation. Rescaling by a factor *Q* preserves the influx of mutations per generation (since $N \mu = (N/Q) \mu Q$). One rescaled generation is *Q* original generations, so this implies a lower influx of mutations per unit of time, but since mean TMRCA scales with *N*, genetic diversity at neutral sites is preserved. Since the probability of fixation of a beneficial mutation scales with *s*, the influx of successfully established beneficial mutations per unit time is preserved (since $N \mu s \, dt = (N/Q) \mu Q s Q (dt/Q)$), implying a smaller number of fixed selected mutations since the mean TMRCA in the population. Since rescaled values of *s* are larger, this has the net effect of substituting many mutations of small effect with a single one of large effect (with $Q = 100$, replacing 100 mutations with $s = 0.001$ by a single one of $s = 0.1$), a very different model of adaptation.

While it may be tempting to always rescale any given scenario to a very small population size, then, one must be careful that finite-size effects do not distort results too much. It is therefore generally advisable to test any rescaled scenario at larger and smaller sizes in order to make sure that the results are consistent. When tree-sequence recording can be used to speed up a simulation, by allowing simulation of neutral mutations to be deferred (see section16.2), or even by allowing the coalescent to be used for neutral burn-in with recapitation (see section 16.10), that will usually be strongly preferable, since tree-sequence recording does not introduce such artifacts. Nevertheless, since tree-sequence recording may not be applicable to a given model, or may provide insufficient performance enhancement, rescaling is still sometimes needed. Rescaling may be used in conjunction with tree-sequence recording, with the appropriate adjustment of parameters such as *μ* and *r* for mutation overlay and recapitation.

As an example of the use of rescaling, consider the following recipe, in which we model neutral and deleterious mutations occurring over a `10` kb locus in a population of initial size `5000`. In generation `50000`, the population experiences a bottleneck that lasts for `5000` generations. A random population sample is then taken in generation `60000`:

```
initialize() {
    initializeMutationRate(1e-8);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "f", -0.01);
    initializeGenomicElementType("g1", c(m1,m2), c(0.8,0.2));
    initializeGenomicElement(g1, 0, 9999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 5000); }
50000 { p1.setSubpopulationSize(1000); }
55000 { p1.setSubpopulationSize(5000); }
60000 late() { p1.outputSample(10); }
```

The patterns of diversity observed in the population sample retrieved at the end of the simulation should be very similar to those obtained from the following recipe, in which we downscaled the population size by a factor of ten:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "f", -0.1);
    initializeGenomicElementType("g1", c(m1,m2), c(0.8,0.2));
    initializeGenomicElement(g1, 0, 9999);
    initializeRecombinationRate(1e-7);
}
1 { sim.addSubpop("p1", 500); }
5000 { p1.setSubpopulationSize(100); }
5500 { p1.setSubpopulationSize(500); }
6000 late() { p1.outputSample(10); }
```

Note how the population sizes, times, mutation rates, recombination rates, and selection coefficients were all rescaled in this scenario. On a 2.26 GHz Intel Xeon Mac Pro running the models in SLiMgui, the first recipe runs in 218 seconds, whereas the second runs in 12 seconds – quite a significant difference.

One caveat is that if the original model uses very high recombination rates, those rates should not be scaled in the simple multiplicative fashion described above. In particular, consider that a recombination rate of `0.5` represents completely independent assortment from one base to the next, due to a probability of crossover between bases of `0.5` (see section 21.1's documentation of `initializeRecombinationRate()`). If a model uses a rate of `0.5` between sites, a rescaled version of that model would still use a rate of `0.5` between those sites, because completely independent assortment can't get *more* independent; indeed, if the rescaling factor were, e.g., `10`, then multiplying the original recombination rate by the rescaling factor would result in a nonsensical scaled rate of `5.0` that would not even be interpretable as a probability. In point of fact, the simple multiplication of rates when rescaling a model is always just an approximation, but for rates less than `0.001` and rescaling factors of `10.0` or less it will be such a close approximation that the difference shouldn't matter. The correct formula for rescaling of recombination rates in SLiM, that gives the rescaled, per-locus recombination rate r_{scaled} corresponding to an original per-locus recombination rate of r with a rescaling factor of n, is (thanks to Peter Ralph):

$$r_{scaled} = \frac{1}{2}(1 - (1 - 2r)^n)$$

For small values of r this produces an essentially linear scaling by n, but as r approaches `0.5` the scaling saturates in the desired manner. For an original rate of `0.001` and a rescaling factor n of `10`, this suggests a rescaled recombination rate of `0.00991`, which is only very slightly lower than the rate of `0.01` produced by naive multiplication. If the original rate were `0.01`, however, the rescaled rate would be `0.0915`, almost 10% off from the rate of `0.1` provided by naive multiplication.

This formula is based upon the probability that a binomial draw will be odd; as a region of length n squeezes down to a single site, the important question for rescaling the recombination rate is the probability that the original region of length n would have an even number of recombination events (cancelling out to produce no effect, once rescaled) or an odd number of recombination events (producing the same effect as a single crossover, once rescaled). In practice, however, if you are rescaling a model in a parameter regime where the effects of this formula matter to your results (besides the fact that a rate of `0.5` should stay `0.5` to produce independence), you may be pushing the limits of safe rescaling, and should proceed with extreme caution. See section 13.18 for a somewhat unusual application of this formula to scaling one particular region of the chromosome in a model.

6. Sexual reproduction

The standard model of reproduction in SLiM assumes (1) hermaphroditic diploid individuals, (2) reproduction by biparental sexual mating, (3) a uniform rate of crossing over without gene conversion during recombination, and (4) modeling of an autosome rather than a sex chromosome. In this chapter, we will explore how each of these assumptions can be modified to study various other scenarios of reproduction. The only limitations are that SLiM remains restricted to diploid organisms (but haploids can be simulated with some creative scripting; see the recipe in section 13.13), hermaphroditism or two-sex systems, and X–Y sex chromosome systems.

6.1 Recombination

6.1.1 Crossing over: Making a random recombination map

Section 4.1.6 introduced the `initializeRecombinationRate()` method in our basic neutral simulation. That section also discussed the possibility of supplying different recombination rates for different stretches of the chromosome, since `initializeRecombinationRate()` takes a vector of rates and a vector of end positions.

Here, then, let's examine a recipe for setting up random variation in the recombination rate along a chromosome, to simulate the presence of "hot spots" and "cold spots":

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);

    // 1000 random recombination regions
    ends = c(sort(sample(0:99998, 999)), 99999);
    rates = runif(1000, 1e-9, 1e-7);
    initializeRecombinationRate(rates, ends);
}
1 { sim.addSubpop("p1", 500); }
10000 { sim.simulationFinished(); }
```

First of all, please note that this recipe is *not empirically based*; the choice of `1000` recombination regions, and the choice of uniform distribution from which the recombination rates are drawn, are both arbitrary. However, it would be straightforward to tailor this recipe to match whatever empirical information about recombination rates and regions one might have.

Let's look at how this code works. Everything new is in the `initialize()` callback, under the comment "`// 1000 random recombination regions`". The `initializeRecombinationRates()` call sets all of the rates in one fell swoop, using a vector named `rates` that contains the recombination rates (in recombination events per base pair per generation), and a vector named `ends` that contains the ends of the recombination regions (in base pairs along the chromosome). Each of these vectors has `1000` elements.

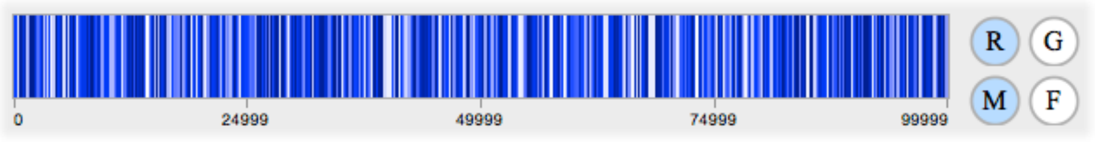
The previous script line creates the `rates` vector by calling the `runif()` function of Eidos. This function generates random draws from a specified uniform distribution. The first parameter requests `1000` samples; the next two parameters give the minimum and maximum values for the uniform distribution to be used. Note that Eidos has several other functions for drawing from other distributions, such as `rnorm()` for a normal distribution, `rpois()` for a Poisson distribution, `rbinom()` for a binomial distribution, and `rexp()` for an exponential distribution. Using these facilities, it is quite easy to make simulations based upon some sort of random configuration or behavior, as in this recipe.

Continuing to work backwards, the preceding script line sets up the vector of recombination region endpoints:

```
ends = c(sort(sample(0:99998, 999)), 99999);
```

Let's analyze this from the inside out. The innermost call is `sample(0:99998, 999)`. The Eidos function `sample()` returns a random sample from a given vector. The given vector here is the sequence `0:99998`, containing every base pair position along the chromosome except for the very last position (for reasons we will see momentarily). The second parameter requests `999` samples. The `sample()` function draws its samples without replacement by default, which is what we want; each recombination region should end at a different base pair. Next, the result from `sample()` is passed to the `sort()` function, which sorts the vector (because `initializeRecombinationRates()` requires the vector of end positions to be in sorted order). Finally, the `c()` function is used to concatenate the value `99999` onto the end of the vector, providing the final entry for the vector; this is the reason that only `999` samples were drawn, from positions up to only `99998`. The last end position is required by `initializeRecombinationRates()` to be the last position in the chromosome.

If we paste this recipe into SLiMgui and do a Recycle and a Step, the random recombination map is loaded into the simulation. To see that it has worked, click the Ⓡ button to turn on display of rate maps (for recombination and mutation – in this case, just recombination, since that is the rate map that has been set). The chromosome view should then show you something like this:



The regions shown in the darkest blues are cold spots, with low rates closer to 10^{-9}, whereas the regions shown in shades close to white are hot spots, with high rates closer to 10^{-7}. Remember that you can drag out a display range in the upper chromosome view, which changes what you see in the lower chromosome view – including the recombination map.

Note that SLiM also allows the recombination map to be tailored at an individual level using a `recombination()` callback; see sections 13.5 and 21.5. Also, note that a mutation rate map may be configured in exactly the same way as this recipe's recombination rate map, using `initializeMutationRate()`.

6.1.2 Crossing over: Reading a recombination map from a file

Rather than generating a random recombination map, you might want to read in and use an empirically determined recombination map such as the map from *Drosophila melanogaster* presented by Comeron et al. (2012) (dataset available in Fiston-Lavier & Petrov 2013). Let's work with chromosome arm 2L, which looks like this:

```
1   0
100001 0
200001 0
300001 0.234550139
400001 0.234550139
500001 1.993676178
...
22800001  0.234550139
22900001  0
23000001  0
```

The length of the 2L arm is given as 23011544 bases; positions in SLiM will thus range from 0 to 23011543 (always beware of off-by-one errors!). The file gives start positions in bases, beginning with 1, with rates in the second column in cM/Mbp (centimorgans per megabasepair). We have a little format conversion to do, but reading this file in and using it in SLiM is quite straightforward:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 23011543);

    // read Drosophila 2L map from Comeron et al. 2012
    lines = readFile("/Users/bhaller/Desktop/Comeron_100kb_chr2L.txt");
    rates = NULL;
    ends = NULL;

    for (line in lines)
    {
       components = strsplit(line, "\t");
       ends = c(ends, asInteger(components[0]));
       rates = c(rates, asFloat(components[1]));
    }

    ends = c(ends[1:(size(ends)-1)] - 2, 23011543);
    rates = rates * 1e-8;
    initializeRecombinationRate(rates, ends);
}
1 { sim.addSubpop("p1", 500); }
10000 { sim.simulationFinished(); }
```

The action is in the initialize() callback after the comment, as before. The first line calls the readFile() function of Eidos to read in a text file at the given filesystem path; you will need to change this path to the correct path to the file on your computer. The result of readFile() is a string vector of lines; each line in the input file becomes a separate string-element.

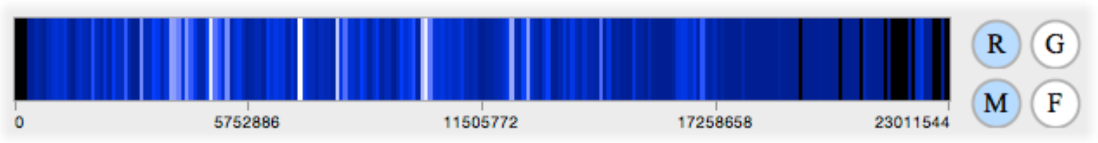
Next, we set rates and ends both to NULL. These will be the rates and endpoints vectors that we will give to SLiM; we will add entries to them one at a time as we process each line in the input file. NULL is a special type indicating "no value"; it often provides a good initial state.

Now comes a loop over the lines read from the file; each line is placed into the loop index variable line, and that line is then processed by the loop body. The strsplit() call splits the line into substrings separated by tab ("\t") characters; since each line has two values separated by a tab, components end up as a string vector of length 2. The next two lines handle those two components by converting them to the correct type and then concatenating them on to the tail of ends and rates using the c() function. This method of building a vector by successive concatenation is a common quick-and-dirty approach, although it is not terribly fast. When the loop finishes, we have rates and positions as specified by the input file.

Finally, we need to convert that data into the format expected by SLiM. The input file specifies start positions, but we want end positions. The expression ends[1:(size(ends)-1)] thus strips off the first value, the start position 1, which is not needed. The -2 correction accomplishes two things: (1) it shifts from starts to ends (each region ends at the base position one less than the base position at which the next region starts), accounting for -1, and (2) it shifts from the 1-based system of the input file, in which the first base is at position 1, to the 0-based system of SLiM, in which the first base is at position 0, accounting for another -1. Finally, the c() call adds the last base position, 23011543, to the tail of the vector.

The second conversion line just converts the recombination rates from cM/Mbp to a rate per base pair per generation, as used by SLiM, by multiplying by 10^{-8}, a conversion ratio that comes from the units involved. 1 cM means that there is a probability of 0.01 of crossover during meiosis. Therefore, 1 cM/Mbp = 10^{-6} cM/bp = 10^{-8} probability of crossover per base pair.

If you paste this recipe into SLiMgui, Recycle, Step, and turn on display of rate maps in the chromosome view with the Ⓡ button, you should see something like this:



This is the *Drosophila* 2L recombination map according to Comeron et al. (2012). Note that a mutation rate map could be read in and set up in SLiM in much the same manner.

6.1.3 Gene conversion

In addition to crossing over, recombination can also lead to gene conversion, the copying of a stretch of the genetic sequence from one chromosome to its homologous chromosome (Chen at al. 2007). By default gene conversion is not enabled in SLiM, but it can be turned on easily:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
    initializeGeneConversion(0.2, 25);
}
1 { sim.addSubpop("p1", 500); }
10000 { sim.simulationFinished(); }
```

The `initializeGeneConversion()` call takes two parameters. The first is the fraction of recombination events that will result in gene conversion; here we decide that `0.2` or 20% will. The second is the mean length of the gene conversion tract, in base pairs; here we specify `25`. When a gene conversion event occurs, the length of the converted tract is drawn by SLiM from a geometric distribution with the specified mean. Note that SLiM does not presently support variation in the gene conversion rate along the chromosome; however, gene conversion can be tailored on a per-individual basis using a `recombination()` callback, which would allow much the same thing (see sections 13.5 and 21.5).

6.2 Separate sexes

6.2.1 Enabling separate sexes

Simulations in SLiM involve hermaphroditic individuals by default. If you wish to simulate separate sexes, however, doing so is essentially just the flip of a switch:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
    initializeSex("A");
}
```

```
    1 { sim.addSubpop("p1", 500); }
    10000 { sim.simulationFinished(); }
```

This recipe is identical to the basic neutral recipe from section 4.1, apart from the addition of a call to the function `initializeSex()`:

```
    initializeSex("A");
```

The parameter here specifies the type of chromosome that is to be modeled; `"A"` specifies modeling of an autosome, but it is also possible to model the X or Y chromosome in SLiM (see section 6.2.3).

Once sex is turned on in a simulation, there is no way to turn it off; it is not possible to make a SLiM simulation in which individuals switch between being sexual and being hermaphroditic. A similar effect could probably be produced by modifying the mate choice algorithm, however (see chapter 11).

Having turned sex on, all subpopulations will keep track of male and female individuals separately, and biparental matings will always involve a male parent and a female parent. A few things work a bit differently when sex is enabled; each subpopulation has a sex ratio that can be specified and modified (see section 6.2.2), for example, and selfing (see section 6.3.1) is not allowed when sex is enabled. Usually you will know whether your code is running with sex enabled or disabled, but if you wish to write general-purpose code that works in either environment, the `sexEnabled` property of `SLiMSim` will tell you whether sex is presently enabled.

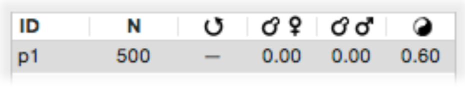
Section 4.2 discussed output of basic simulation state using the `outputFull()` and `outputSample()` methods of `SLiMSim`. When sex is enabled, the output generated by these methods changes slightly. In particular, the `H` symbol that was used to designate individuals as hermaphrodites will change to indicate the sex of each individual with `M` or `F`. In addition, if sex chromosomes are modeled (see section 6.2.3), the `A` that designated genomes in the output as autosomes will change to an `X` or `Y` as appropriate.

6.2.2 Sex ratios

When individuals are one of two sexes, rather than being hermaphroditic, the question of the sex ratio immediately arises. A sex ratio of `0.5` is maintained by default in SLiM; if that is what you want, no further action is required. To set a sex ratio (i.e., male fraction; see below) of `0.6`, on the other hand, you simply supply an extra parameter to `addSubpop()` (or to `addSubpopSplit()`, which works in the same way):

```
    initialize() {
        initializeMutationRate(1e-7);
        initializeMutationType("m1", 0.5, "f", 0.0);
        initializeGenomicElementType("g1", m1, 1.0);
        initializeGenomicElement(g1, 0, 99999);
        initializeRecombinationRate(1e-8);
        initializeSex("A");
    }
    1 { sim.addSubpop("p1", 500, 0.6); }
    10000 { sim.simulationFinished(); }
```

If you paste this recipe into SLiMgui, Recycle, and Step twice to get through generation 1, you can see in the population table view that this sex ratio has been used by SLiM:



ID	N	↺	♂♀	♂♂	◕
p1	500	—	0.00	0.00	0.60

The column labeled ◕ shows the current sex ratio of each subpopulation; the subpopulations in the simulation do not all need to have the same sex ratio. The sex ratio of a subpopulation can be accessed in script through the `sexRatio` property of `Subpopulation`; in the recipe above, for example, `p1.sexRatio` would be equal to `0.6`.

The "sex ratio" in SLiM refers to the *male fraction*, the fraction of the total subpopulation that is male. Symbolically, it is therefore `M/(M+F)`, where `M` and `F` are the number of males and females respectively. A sex ratio of `0` would imply all females; a sex ratio of `1` would imply all males; the default sex ratio of `0.5` is half males and half females.

You are free to set almost any sex ratio you wish; SLiM will raise an error, however, if the simulation is forced into a situation in which a subpopulation would become unisexual (whether due to the sex ratio, cloning rate, or other factors). All subpopulations must be viable, which means that at least one parent of each sex must be available to produce offspring.

It is possible for the sex ratio of a subpopulation to change over time. For example, here is a recipe for a simulation in which the sex ratio fluctuates randomly around 0.5:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
    initializeSex("A");
}
1 { sim.addSubpop("p1", 500); }
1: { p1.setSexRatio(runif(1, 0.3, 0.7)); }
10000 { sim.simulationFinished(); }
```

The `setSexRatio()` method of `Subpopulation` simply takes a `float` representing the new sex ratio. As with `setSubpopulationSize()`, the change is not effected immediately; instead, the call sets the target sex ratio that will be used when offspring are generated. The recipe above draws a new random sex ratio between `0.3` and `0.7` in each generation using `runif()`.

6.2.3 Modeling sex-chromosome evolution

So far we have always seen simulations of autosomal evolution, but SLiM also supports simulation of sex chromosome evolution. The choice of chromosome type is made in the `initializeSex()` call, so to simulate X chromosome evolution one would simply do:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
    initializeSex("X");
}
1 { sim.addSubpop("p1", 500); }
10000 { sim.simulationFinished(); }
```

The `"X"` passed to `initializeSex()` sets SLiM to model the X chromosome. SLiM will handle all of the necessary details; females in the simulation will be XX, whereas males will be XY. Since the Y chromosome is not being modeled in this scenario, it will be a "null chromosome", a placeholder kept by SLiM simply to make the diploid bookkeeping balance. Null chromosomes have no structure, receive no mutations, and raise an error if you attempt to do much of anything with them. It is also possible to supply `"Y"` to `initializeSex()`, to model the Y chromosome; in this case it is the X chromosome that will be a “null chromosome”. If you need to work directly with `Genome` objects in your script (we will see some examples of this later), you can find out whether a given genome is null or not with the `isNullGenome` property of `Genome`.

When modeling sex chromosomes, recombination works as you would expect it to. To be specific, if you are modeling the X chromosome, recombination will occur between the two X chromosomes of female parents when generating their gametes, whereas no recombination will occur between the X and Y chromosomes of a male. If you are modeling the Y chromosome, recombination does not occur, since the X chromosome in this case is a null chromosome, and individuals never possess two Y chromosomes.

When modeling the X chromosome, there are two different ways in which an individual can be heterozygous for a given mutation: the individual might be XX (i.e., female) and possess the mutation on just one X chromosome, or the individual might be XY (i.e., male) and possess the mutation on the one X chromosome present. These cases are handled differently by SLiM when it calculates the fitness effect of a mutation. The first case is handled in the same way as when modeling an autosome: the dominance coefficient for the mutation type of the mutation, as supplied to `initializeMutationType()`, specifies a multiplicative modifier for the selection coefficient of the mutation (see section 4.1.3). The second case is unique to the case of modeling the X chromosome, and is handled using a special *X-dominance coefficient*. This coefficient is `1.0` by default, meaning that an XY individual possessing an X-linked mutation will experience the same fitness effect from that mutation as an XX individual that is homozygous for that mutation (a reasonable assumption because of X inactivation). The X-dominance coefficient may be changed by supplying an optional second parameter to the `initializeSex()` function:

```
    initializeSex("X", 0.8);
```

The `dominanceCoeffX` property of `SLiMSim` can also be used to get and set the X-dominance coefficient; for example, one could vary its value over time. However, this mechanism is presently much less flexible than the standard dominance coefficient, since a single X-dominance coefficient value is used for all mutations in all subpopulations at present. Of course it would be possible to introduce a more complex fitness calculation scheme using a `fitness()` callback, as discussed in chapter 9.

When modeling the Y chromosome, individuals can only possess zero or one copy of a given mutation, since males possess one Y and females possess none. For this reason, SLiM does not use a dominance coefficient at all in this case. The selection coefficient of the mutation determines its fitness effect, and the dominance coefficient supplied in the mutation type is simply ignored.

It is worth noting that the way in which the Y chromosome is modeled in SLiM is in some ways similar to how one might model mitochondrial genomes. If SLiM is used in this way, the XY “males” are really the females, with a single genome possessed by all of the mitochondria in a given female. The XX “females” are really the males; they possess mitochondria too, of course, but they do not pass them down to their offspring, so their mitochondria are an evolutionary dead end that does not need to be modeled. This equivalence should work unless you need to model the fitness effects of mitochondrial mutations in males; that would probably also be possible in SLiM, using an autosomal model with a `modifyChild()` callback, but it is beyond the scope of this manual.

6.3 Selfing and cloning

6.3.1 Selfing in hermaphroditic populations

Selfing, or self-fertilization, is the mating of an individual with itself: male and female gametes from one individual combine to form a zygote. Selfing is different from cloning in that gametes are produced and fertilize, so offspring are not clones of their parent; notably, recombination occurs in selfing. It is an essentially hermaphroditic phenomenon, since hermaphroditic individuals can produce both eggs and sperm, can produce both X and Y gametes, and are fertile. There are probably counterexamples somewhere in biology, where it sometimes seems that anything that is possible exists; but in SLiM, at least, selfing is limited to the hermaphroditic case.

Returning to a hermaphroditic model, then, selfing can be turned on with a single call:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
    p1.setSelfingRate(0.8);
}
10000 { sim.simulationFinished(); }
```

The `setSelfingRate()` method call here on `p1` tells SLiM that selfing should be used to generate 80% of the offspring in subpopulation `p1`. The selfing rate may be anything from `0.0` (the default) to `1.0`. The `setSelfingRate()` method may be called at any time, so the selfing rate can be varied over time or in response to other simulation conditions. The current selfing rate for a subpopulation is shown in the population table view under the ↺ column.

Usually it is not important, but it should be noted that in non-sexual simulations SLiM does not prevent a parent from being chosen twice, as both parents in a biparental mating event. Even when the selfing rate is set to `0`, therefore, a low background rate of selfing may occur. This can easily be prevented if necessary; see the recipe in section 12.4.

6.3.2 Cloning

SLiM also supports clonal reproduction, in which offspring are an exact genetic copy of a single parent (except for new mutations introduced during the copying of the DNA). Indeed, hermaphroditic simulations may have a combination of biparental mating, self-fertilization, and cloning. In a hermaphroditic model, setting up clonal reproduction is a single call:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
    p1.setCloningRate(0.1);
}
10000 { sim.simulationFinished(); }
```

The `setCloningRate()` call here tells SLiM to generate 10% of the offspring in `p1` clonally (the remaining 90% will be generated biparentally as usual). The cloning rate may be anything from `0.0` (the default) to `1.0`. The `setCloningRate()` method may be called at any time, so the cloning rate can be varied over time or in response to other simulation conditions. The current cloning rate for each subpopulation is shown in the population table view under the ♂♀ and ♂♂ columns; in the hermaphroditic case the same number will be shown in both columns (the icon depicts a little Athena budding parthenogenically from the head of Zeus, if that is not immediately obvious).

Clonal reproduction is also supported in the case of separate sexes. It works in essentially the same way:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
    initializeSex("A");
}
1 {
    sim.addSubpop("p1", 500);
    p1.setCloningRate(c(0.5,0.0));
}
10000 { sim.simulationFinished(); }
```

The only difference is that when separate sexes are enabled by `initializeSex()`, the `setCloningRate()` method can take a vector of two rates, as above. Here the cloning rate is set to `0.5` for females, but `0.0` for males, reflecting a somewhat common situation in some taxa, in which females can reproduce parthenogenically but males can reproduce only sexually. You may still pass a singleton value to `setCloningRate()`; when separate sexes are enabled, that value is then taken as the cloning rate for both males and females. The current cloning rates for the females and males in each subpopulation is shown in the population table view under the ♂♀ and ♂♂ columns.

7. Mutation types, genomic elements, and chromosome structure

A number of concepts such as mutation types, genomic element types, genomic elements, and chromosome structure were already introduced in chapter 4 in our basic neutral simulation. Here we return to those foundational concepts and explore them in more detail, showing how simulations might use multiple mutation types, multiple genomic element types, and many genomic elements to simulate more realistic chromosome structures with mutations of varying selective effects.

The structure of this chapter will be a bit different from that of previous chapters. In this chapter each subsection will build upon the recipe introduced by the previous subsection, working towards making a relatively large final recipe for a full-chromosome simulation.

7.1 Mutation types and fitness effects

In section 4.1.3 the concept of a mutation type was introduced: a category of mutations that represents some particular subset of the mutations in a simulation. Examples might include “neutral mutations”, “beneficial mutations introduced by the simulation script in generation 10”, or “mutations that will be forced to sweep to fixation”. Mutation types are represented in SLiM with the `MutationType` class, and each defined mutation type has a unique symbolic identifier of the form `mX`, like `m1` or `m27`. Whenever you want to be able to generate or refer to a particular type of mutations separately from other types, you will want to define a new mutation type.

Section 4.1.3 also introduced the function used to create new mutation types at initialization time, `initializeMutationType()`. This function can only be called inside an `initialize()` callback; in fact, it is not even defined at other times. Mutation types can therefore be set up only at initialization time; you must set up all of the types that your simulation will need for the entire run. After initialization, mutation types are typically static entities; however, there is a method, `setDistribution()`, that may be used to change a mutation type’s distribution of fitness effects, affecting new mutations generated from that point onward.

A mutation type is basically defined by two things: its dominance coefficient, and its distribution of fitness effects (DFE). Both of these properties are important only because they affect new mutations that are generated from a given mutation type: (1) each mutation of a given mutation type receives a selection coefficient drawn from the mutation type’s DFE, and (2) individuals that are heterozygous for a mutation will use the dominance coefficient, obtained from the mutation type of the mutation, to modify the selection coefficient of the mutation.

For the purposes of this recipe, let’s define four mutation types: two for neutral mutations (non-coding and synonymous), one for mildly deleterious mutations, and one for strongly beneficial mutations:

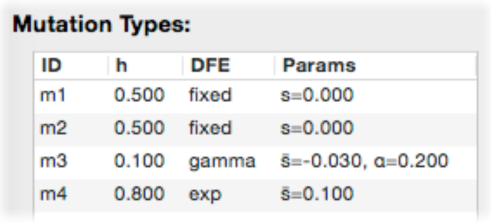
```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);         // non-coding
    initializeMutationType("m2", 0.5, "f", 0.0);         // synonymous
    initializeMutationType("m3", 0.1, "g", -0.03, 0.2);  // deleterious
    initializeMutationType("m4", 0.8, "e", 0.1);         // beneficial
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 5000); }
10000 { sim.simulationFinished(); }
```

The neutral mutation types, `m1` and `m2`, are defined with a dominance coefficient of `0.5` (which does not matter for neutral mutations), and mutations drawn from them receive a fixed selection coefficient (DFE type `"f"`) of `0.0` as specified by the DFE parameter. Note that they are exactly identical in their parameters; however, they will be used to represent different conceptual types of neutral mutations, with `m1` representing neutral mutations in non-coding regions and `m2` representing synonymous mutations in coding regions. Drawing this distinction will allow us to distinguish these two classes of mutations later on, when we are observing the simulation running.

The deleterious mutation type, `m3`, has a dominance coefficient of only `0.1`, meaning that heterozygous individuals feel very little effect from these mutations; they are almost recessive. These mutations are drawn from a gamma distribution (see section 21.9) with a mean of `-0.03`, with a shape parameter (alpha) of `0.2`.

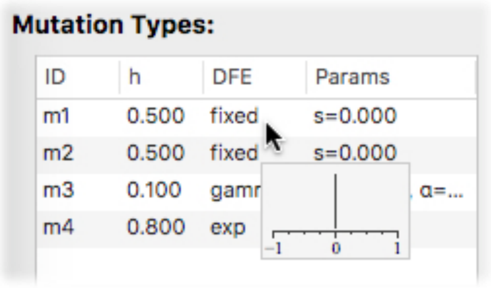
Finally, the beneficial mutation type, `m4`, has a dominance coefficient of `0.8`, representing incomplete dominance. Mutations of this type are drawn from an exponential DFE with a mean of `0.1`.

All defined mutation types can be viewed in the drawer on the simulation window. If you paste in the recipe so far, Recycle, and Step, then open the drawer by pressing the ☞ button, you can see the mutation types listed, which can be quite useful if mutation types are manufactured *en masse* with a `for` loop or similar automated construction method:


Mutation Types:

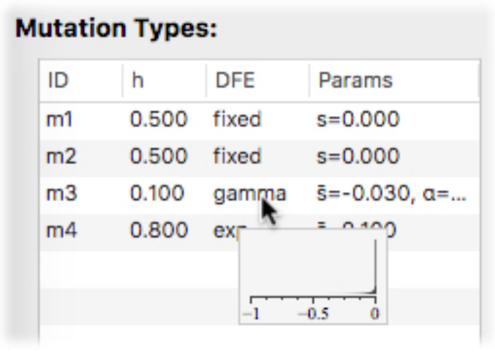
ID	h	DFE	Params
m1	0.500	fixed	s=0.000
m2	0.500	fixed	s=0.000
m3	0.100	gamma	s̄=-0.030, α=0.200
m4	0.800	exp	s̄=0.100

We are not using the new mutation types yet, just defining them; we'll make more progress with this recipe in the next section. Before we move on to that, however, there is one hidden feature worth mentioning. The mutation type table that is depicted in the screenshot above has a nice hidden addition: tooltips that show the mutation type's DFE graphically. If you place the mouse cursor over the `m1` line without moving it for a second or a bit more (often called a "hover" of the cursor), a "tooltip" – a little informational tab – will appear:


Mutation Types:

ID	h	DFE	Params
m1	0.500	fixed	s=0.000
m2	0.500	fixed	s=0.000
m3	0.100	gamr	α=...
m4	0.800	exp	

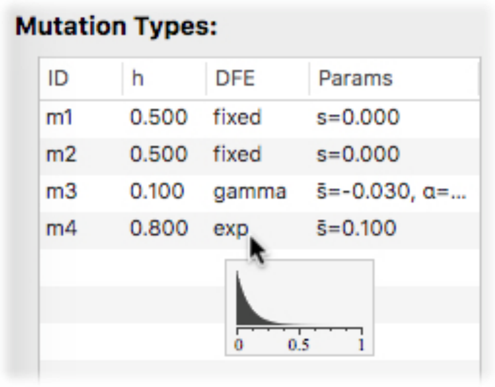
(Ignore the somewhat different appearance of the two screenshots above; they were taken on different versions of OS X, and Apple changed the standard system font and other aspects of table appearance from one OS X release to the next.) The tooltip shown above contains a plot of the mutation type's distribution of fitness effects; the *x*-axis is the selection coefficient, and the *y*-axis is the distribution's relative density. In this case, since the mutation type has a fixed selection coefficient of `0.0`, the distribution consists of a single peak at `0.0`. Hover over `m3`, and a more interesting tooltip appears:


Mutation Types:

ID	h	DFE	Params
m1	0.500	fixed	s=0.000
m2	0.500	fixed	s=0.000
m3	0.100	gamma	s̄=-0.030, α=...
m4	0.800	ex	s̄=0.100

This plot shows the specific gamma distribution specified by the parameters for `m3`; note that the *x*-axis now spans the range –1 to 0 only, since this DFE does not include any positive selection coefficients. The distribution shown has most of its density very close to zero, but a tail is visible extending downward perhaps as far as –0.25.

Hovering over `m4` shows its DFE:


Mutation Types:

ID	h	DFE	Params
m1	0.500	fixed	s=0.000
m2	0.500	fixed	s=0.000
m3	0.100	gamma	s̄=-0.030, α=...
m4	0.800	exp	s̄=0.100

This is a non-negative DFE, so the *x*-axis spans 0 to 1, and this distribution is much broader. This sort of visualization can prove quite helpful in configuring and debugging DFEs.

7.2 Genomic element types

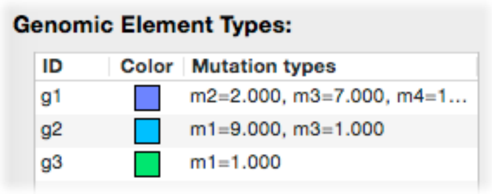
Now that we have a couple of mutation types defined, we can make some genomic element types that use these mutation types. Genomic element types were introduced in section 4.1.4; they represent a type of region in the genome with a particular mutational profile. For this simple toy model, let's focus on exons, introns, and non-coding regions:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);        // non-coding
    initializeMutationType("m2", 0.5, "f", 0.0);        // synonymous
    initializeMutationType("m3", 0.1, "g", -0.03, 0.2); // deleterious
    initializeMutationType("m4", 0.8, "e", 0.1);        // beneficial
    initializeGenomicElementType("g1", c(m2,m3,m4), c(2,8,0.1));  // exon
    initializeGenomicElementType("g2", c(m1,m3), c(9,1));       // intron
    initializeGenomicElementType("g3", c(m1), 1);        // non-coding
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 5000); }
10000 { sim.simulationFinished(); }
```

Genomic element type `g1` defines exons, which often suffer deleterious mutations, sometimes get neutral (synonymous) mutations, and very rarely get beneficial mutations. Type `g2` defines introns, which often get neutral (non-coding) mutations, and occasionally get deleterious mutations. Type `g3` defines non-coding regions, which get neutral (non-coding) mutations only. Each genomic element type is defined with a call to `initializeGenomicElementType()`, as previously discussed in section 4.1.5; its parameters supply the identifier for the new type, a vector of mutation types, and a vector of relative proportions for those mutation types among the new mutations that occur in the genomic elements of this type.

Notice that there is *not* a one-to-one correspondence between mutation types and genomic element types; this is typical, since the two classes represent quite different objects. A genomic element often draws from a variety of different mutation types, with various probabilities. If this model were expanded to be more biologically realistic, it might have quite a few more genomic element types (3′ and 5′ UTRs, promoters and enhancers and silencers, various different types of non-coding regions...) but might have only a couple more mutation types (a strongly deleterious mutation type, to represent things like premature stop codons and broken promoters, for example).

Again, this recipe is not yet complete; now that we have defined genomic element types we need to make genomic elements that use those types. However, at this point we can Recycle, Step, and observe the defined genomic element types in the simulation window's drawer:


Genomic Element Types:

ID	Color	Mutation types
g1	🟦	m2=2.000, m3=7.000, m4=1...
g2	🟦	m1=9.000, m3=1.000
g3	🟩	m1=1.000

Note that each genomic element type is automatically assigned a color by SLiMgui. We will soon see how these colors are used.

7.3 Chromosome organization

As previously discussed in section 4.1.5, genomic elements are regions of a chromosome that use a particular genomic element type. The genomic element types define what possibilities exist in the chromosome; the genomic elements determine what actually does exist. Having defined genomic element types for exons, introns, and non-coding regions, we now need to create genomic elements to express how the genomic element types are distributed in the chromosome.

As has been the case all along with this recipe, the goal here is not biological realism; nevertheless, it is interesting to try to come up with a recipe that broadly approximates the structure of a real chromosome, just to show how the problem might be approached. In this recipe, then, the formulas used for the lengths of exons and introns are very loosely based on empirical length distributions.

This is by far the longest recipe we've seen so far, so a bit of preamble to prepare the way for it is helpful. We have previously used `for` loops to iterate over a specified vector. This example uses two new looping constructs, a `do` loop and a `do–while` loop. These both iterate as long as a given condition remains true; when the conditions tests false, the loop terminates. The only difference between them is that `do–while` tests its condition at the end of the loop body, and thus the loop body always executes at least once. The other new thing in this recipe is use of the `rlnorm()` function, which draws samples from a lognormal distribution. In addition to the number of samples to draw, it takes the mean and standard deviation of the distribution as parameters, on the log scale. With that preface, here is the recipe:

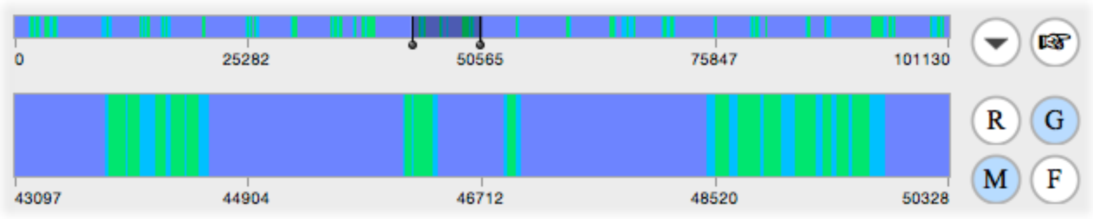
```
initialize() {
    initializeMutationRate(1e-7);

    initializeMutationType("m1", 0.5, "f", 0.0);         // non-coding
    initializeMutationType("m2", 0.5, "f", 0.0);         // synonymous
    initializeMutationType("m3", 0.1, "g", -0.03, 0.2);  // deleterious
    initializeMutationType("m4", 0.8, "e", 0.1);         // beneficial

    initializeGenomicElementType("g1", c(m2,m3,m4), c(2,8,0.1));  // exon
    initializeGenomicElementType("g2", c(m1,m3), c(9,1));       // intron
    initializeGenomicElementType("g3", c(m1), 1);           // non-coding

    // Generate random genes along an approximately 100000-base chromosome
    base = 0;

    while (base < 100000) {
      // make a non-coding region
      nc_length = asInteger(runif(1, 100, 5000));
      initializeGenomicElement(g3, base, base + nc_length - 1);
      base = base + nc_length;

      // make first exon
      ex_length = asInteger(rlnorm(1, log(50), log(2))) + 1;
      initializeGenomicElement(g1, base, base + ex_length - 1);
      base = base + ex_length;

      // make additional intron-exon pairs
      do
      {
        in_length = asInteger(rlnorm(1, log(100), log(1.5))) + 10;
        initializeGenomicElement(g2, base, base + in_length - 1);
        base = base + in_length;

        ex_length = asInteger(rlnorm(1, log(50), log(2))) + 1;
        initializeGenomicElement(g1, base, base + ex_length - 1);
        base = base + ex_length;
      }
      while (runif(1) < 0.8);  // 20% probability of stopping
    }

    // final non-coding region
    nc_length = asInteger(runif(1, 100, 5000));
    initializeGenomicElement(g3, base, base + nc_length - 1);

    // single recombination rate
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 5000); }
10000 { sim.simulationFinished(); }
```

This is too much code to parse through line by line, but it should be fairly clear what is going on. The outer loop adds one non-coding region and then one gene each time that it iterates; the inner loop adds one intron-exon pair with each iteration. The overall algorithm is not targeted to end at a fixed chromosome length (doing that without biasing the metrics of the final gene generated would be a bit tricky); instead, genes are added until the chromosome length exceeds `100000` and then the process is ended with a final non-coding region. Eidos does not have any built-in facility for graphing, so you can't directly see the distributions used to generate the lengths of the exons and introns; however, since the syntax of Eidos is so similar to that of R, it is quite easy to use R to plot these distributions. The only hitch is that conversion to integer is `asInteger()` in Eidos but `as.integer()` in R, so that has to be tweaked. If you are so inclined, try running this code in R:

```
x = as.integer(rlnorm(100000, log(50), log(2))) + 1
hist(x[x < 250], breaks=100)
```

That will produce a plot of the distribution of exon lengths, which may be compared to the distribution shown in Deutsch & Long (1999), which was loosely used as a reference for this model. The distribution of intron lengths may be compared similarly.

If you paste in the recipe above, Recycle, and Step, you will see the random chromosome structure that it generated, which might look something like this (after turning on display of genomic elements with the Ⓖ button, and selecting a subrange in the upper chromosome view to show some detail):



The structure of non-coding regions (purple) interspersed with genes made up on exons (blue) alternating with introns (green) appears to be as intended. It should now be clear, of course, how SLiMgui uses the colors that it assigns to genomic element types, as seen in the previous section.

Rather than generating a random chromosome organization, you might wish to read in an actual chromosome map and generate genomic regions based upon that information, to simulate the evolution of a particular organism. That is left as an exercise for the reader, but with the recipe in section 6.1.2 as guidance it should not be too difficult.

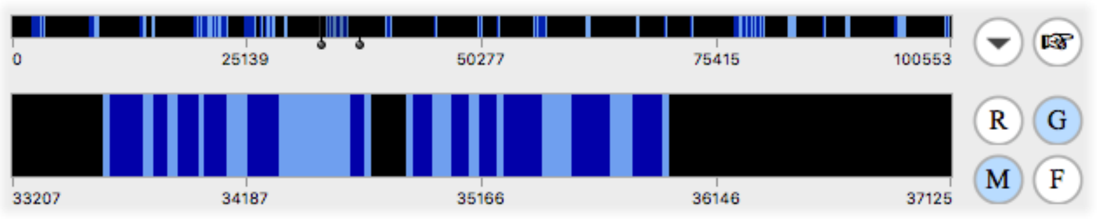
7.4 Custom display colors in SLiMgui

The model that we built in the previous three sections uses various default colors schemes supplied by SLiMgui: mutations are colored according to their selection coefficients, genomic element types are automatically assigned colors from a standard palette, and individuals are colored according to their fitness. For simple models these default colors generally suffice, but when constructing complex models it may be helpful to customize the color scheme used in SLiMgui to improve the clarity of the models' visual representation. In this section we will briefly explore SLiM's facilities for doing so.

First of all, the colors used for genomic regions, as shown in the figure above in section 7.3, is perhaps less than ideal. It would be nice if non-coding regions were shown in a distinctive color suggestive of the unimportance of those regions to the organism, such as black. Similarly, perhaps exons could be in the brightest color, connoting their importance, whereas introns could be shown in a more muted fashion. This can be accomplished by simply adding these lines after the calls to `initializeGenomicElementType()` have set up the genomic element types:

```
g1.color = "cornflowerblue";
g2.color = "#00009F";
g3.color = "black";
```

This produces a chromosome view like this:



It works by setting values on the `color` property of the genomic element types. By default, these `color` properties are the empty string, `""`, which tells SLiM to use a color from its default color palette. Here we have instead told SLiM to use a light blue named `"cornflowerblue"` for the exons represented by `g1`, and `"black"` for non-coding regions represented by `g3`. These names are two of the 657 named colors supported by SLiM. The complete list of named colors is identical to the named color list provided by the R language, for simplicity, and so there are various web resources available that show all of the names and their corresponding colors (one such resource: http://research.stowers-institute.org/efg/R/Color/Chart/ColorChart.pdf). You can browse such a list, and then simply use the name for the color you want in SLiM.

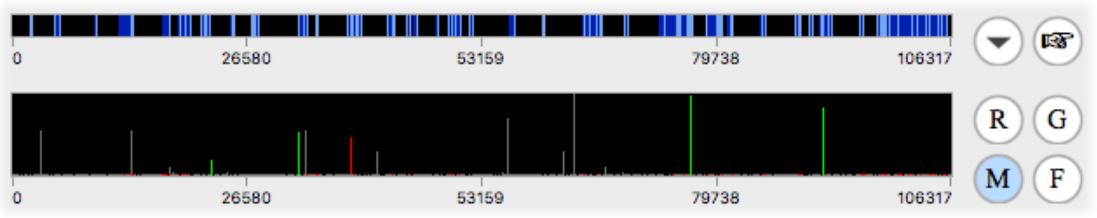
The color used for `g2` is not a named color, however; instead, it is the rather cryptic string value `"#00009F"`. This specifies the color in hexadecimal, or base 16, as two-digit values for the red, green, and blue components of the color. With values of zero for red and green, and a value of `9F` for blue, this string represents a dark blue that works well for introns here.

The Eidos manual has further discussion of how colors are specified in SLiM (this is actually part of the Eidos language). Note that setting colors on SLiM objects in this way only has an effect in SLiMgui, but it is entirely legal when running SLiM models at the command line; the properties still exist, but are unused by SLiM outside of SLiMgui.

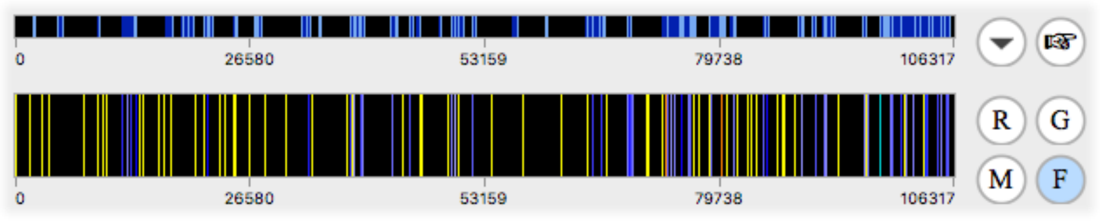
Now that the genomic elements are colored nicely, let's set up new colors for the mutations. By default, SLiMgui displays neutral mutations in yellow, beneficial mutations in shades of green and blue, and deleterious mutations in shades of orange and red. Let's suppose we want to de-emphasize neutral mutations in this model; we want them to display, but in a less visible color than the default bright yellow color. We also want all beneficial mutations to be a single shade of green (the blue doesn't show up well against the blues we've chosen for our genomic elements), and we want all deleterious mutations to be bright red so we can see them very clearly. This can be achieved with a few lines placed after the mutation types have been defined:

```
m1.color = "gray40";
m2.color = "gray40";
m3.color = "red";
m4.color = "green";
```

That produces a display like this (with display of the genomic elements turned off now, for greater clarity):



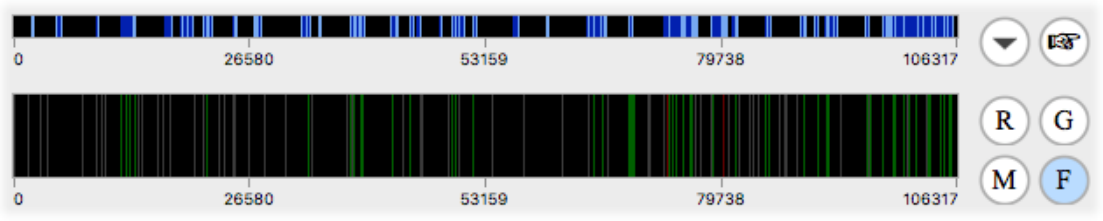
That looks like what we had in mind. If we turn on display of fixed mutations instead of segregating mutations, however, we see that those are still being displayed in SLiM's default color scheme:



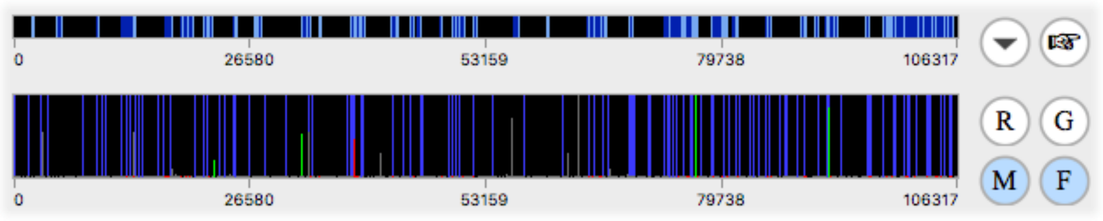
This is obviously not what we want. Instead, let's use darker shades of the same colors used for the mutations when they are still segregating. This can be done by setting the colorSubstitution property of the mutation types:

```
m1.colorSubstitution = "gray20";
m2.colorSubstitution = "gray20";
m3.colorSubstitution = "#550000";
m4.colorSubstitution = "#005500";
```

That produces the desired result:



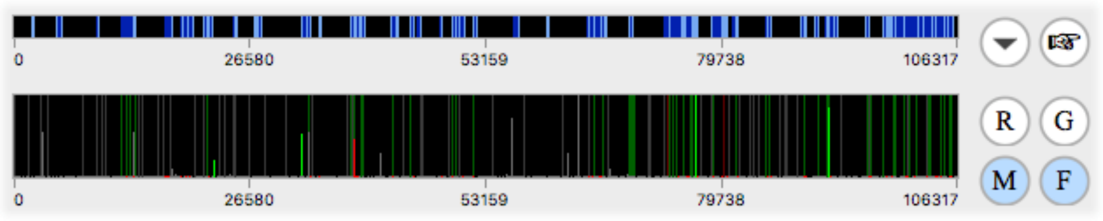
There's one thing left for us to tweak. If we turn on display of both segregating and fixed mutations, SLiMgui displays the fixed mutations using a shade of blue, rather than the colors we just set up above:



This is deliberate, to prevent too much clutter and chaos in the chromosome view. However, we deliberately chose dark colors above for our fixed mutations with the intention of having them coexist aesthetically, so we'd like to tell SLiMgui to use our color scheme in all cases. The default dark blue color SLiMgui uses for fixed mutations when both are being displayed is a property on the Chromosome object named colorSubstitution. By default, it is set to "#3333FF", the dark blue color being used. We can set it to the empty string, "", instead; this eliminates the use of this default color. Since the Chromosome object is not available until the simulation has been fully initialized, we can do this at the beginning of generation 1, by adding a line to the generation 1 event:

```
sim.chromosome.colorSubstitution = "";
```

Now our model displays as intended:



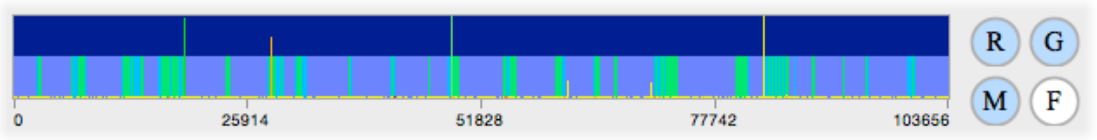
The fixed mutations are now in dark, dimmed colors, whereas the currently segregating mutations are in bright, clear colors that are easily visible against that background.

We won't give an example of it here, but the `Individual` class in SLiM also has a `color` property that can be set to override the default fitness-based color scheme for display of individuals. Setting this property should be done in a `late()` event, since SLiMgui updates its display at the very beginning of each generation; `early()` events are executed after SLiMgui has already displayed, and so setting display colors for individuals at that time will have no visible effect. Generally SLiMgui's fitness-based coloring works well, but in some special cases it might be useful to give a specific color to individuals that possess some particular property – especially in models in with the `tag` values of individuals are being used to keep track of extra state information.

8. SLiMgui visualizations for polymorphism patterns

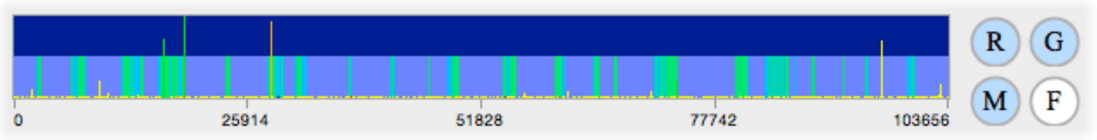
The previous chapter developed a model of evolutionary dynamics in a scenario involving neutral, deleterious, and beneficial mutations. Given the full recipe from section 7.3 (*not* 7.4) of the previous chapter, we will look briefly in this chapter at the interplay of selection, drift, and hitchhiking when it executes, since it's the most complex model we've made thus far.

First of all, if you Recycle and Play, you should see a fairly complicated dance of mutations, some fixing quickly, others struggling, but most flickering in and out of existence quickly:



Notice that display of rate maps has been turned on with the Ⓡ button; otherwise, the genomic elements display spans the full view height and makes it hard to see mutations that are at high frequency. Notice also that the mutation lines are distinct colors; neutral mutations are yellow, beneficial are green, and deleterious are orange or sometimes even red. You might need to play with the selection coefficients color scale slider (see section 3.1) to optimize these colors.

A cloud of neutral and deleterious mutations occupies the bottom row of pixels; most mutations in the model are neutral or deleterious. A few beneficial mutations are visible in green, near `19000` and `48000`. A neutral mutation near `83000` and a deleterious mutation near `29000` have been dragged up to high frequency by the two beneficial mutations they are linked to, both of which are about to fix. A few dozen generations later, this is the situation:

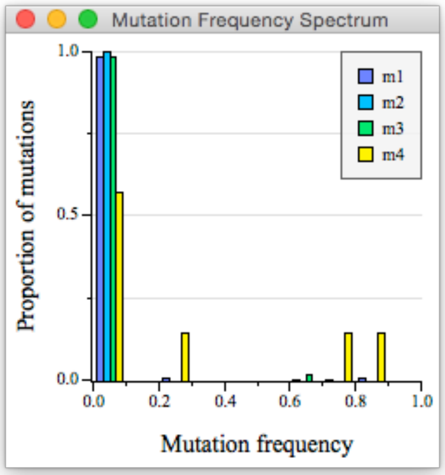


The beneficial mutation near `48000` has fixed, and is thus no longer displayed. The one near `19000` has not yet fixed, but a new beneficial mutation has arisen near `17000` on top of both the beneficial mutation near `48000` and the deleterious mutation near `29000`. With that added selective pressure, the deleterious mutation has risen near fixation. After another couple of dozen generations, however, recombination produced a new variant containing the beneficial mutation without the deleterious mutation. That variant rose very quickly, fixing the beneficial mutation while leaving the deleterious mutation at a frequency of only ~0.5. It then dropped and was lost fairly quickly, no longer having the benefit of its linked companions. In this model it is fairly rare for a deleterious mutation to make it all the way to fixation, although it does occasionally happen.

As the simulation is running, you can watch the colors of the individuals, shown in the top center view, to see the mix of different fitnesses present. As a beneficial mutation sweeps, more and more individuals will turn green (if the fitness color scale slider is set appropriately); once the mutation fixes, they will suddenly revert toward yellow, since the fitness benefit of that mutation is no longer part of SLiM's fitness calculations.

8.1 Mutation frequency spectra

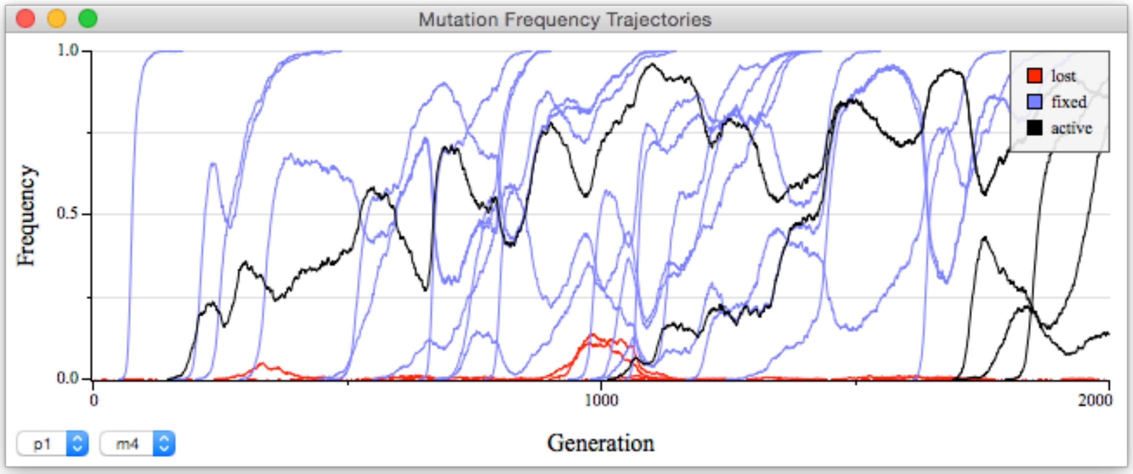
SLiMgui has a number of graphs it can display to help analyze and understand the simulation. While running this recipe, for example, if you click the 📊 button and select "Graph Mutation Frequency Spectrum" you should see something like this:



Remember that `m1` and `m2` are neutral, `m3` is deleterious, and `m4` is beneficial. What this plot tells us is that out of all mutations that are of type `m1`, for example, the vast majority are at very low frequency; the same is true of `m2` and `m3`. Out of all mutations that are of type `m4`, however – the beneficial mutations – a fairly large proportion are at middle or high frequency, because they are on their way to fixation.

8.2 Mutation frequency trajectories

The next graph in SLiMgui's graph menu is "Graph Mutation Frequency Trajectories". Whereas the previous graph showed us only an analysis of the frequencies of different mutation types at the present moment in time (try opening it while the simulation is actually playing), this graph shows us similar information across the whole run of the model so far:



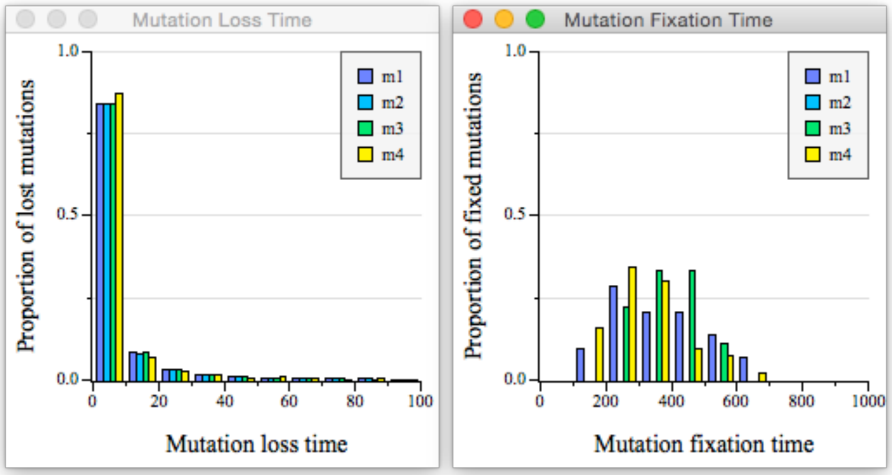
Using the popups at the lower left of the window, you can select a particular subpopulation and mutation type. The data collected for this graph can be quite large, and quite slow to collect. For this reason, the data are not normally collected when you run a model; doing so would slow SLiM down too much. Instead, the data are collected only when the graph window is open, and only for the subpopulation and mutation type chosen. If you want a plot for an entire simulation run, as shown above, you should therefore (1) Recycle, (2) Step once to advance to generation `1`, (3) open the graph window, (4) select the mutation type you want from the popup, and (5) press Play to run your simulation with data collection.

The result at the end of a simulation run might look something like the graph shown above. The complete trajectory of every mutation of the selected mutation type in the selected subpopulation is shown with an individual curve in this plot; here we're looking at beneficial mutations (type `m4`), and there is only one subpopulation. The color of each curve indicates whether the mutation was lost (red), fixed (blue), or is still segregating (black).

SLiMgui provides various options to configure the visual appearance of plots. If you control-click or right-click on the graph window here, for example, you will get a context menu with menu items that allow you to show/hide grid lines, show/hide the legend, and so forth. If you're following along in SLiMgui, try experimenting with these options; you can't do any harm. SLiMgui graph windows also make their data available to you, if you want to regenerate them or perform further analysis; from the context menu, just select "Copy Data" to copy the underlying data for the plot to the clipboard, or "Export Data..." to export the data to a text file readable by other programs such as R. The format of the data should be pretty self-explanatory.

8.3 Times to fixation and loss

Next let's look at the plots for "Graph Mutation Loss Time Histogram" and "Graph Mutation Fixation Time Histogram", side by side:

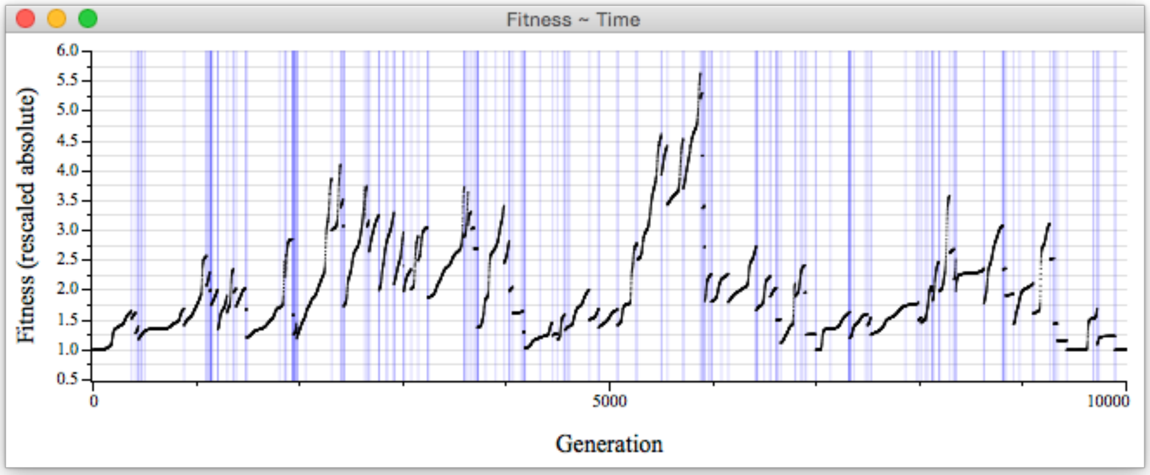


These plots show an analysis of metrics gathered over the course of the entire run. The loss time plot, on the left, shows the distribution of loss times, in generations, for each of the four mutation types. The loss profile for all four types is quite similar. Remember that this is *not* saying that beneficial mutations are just as likely to be lost as deleterious mutations, but only that *when* a beneficial mutation is lost, the amount of time it takes to be lost is similar to the amount of time it takes a deleterious mutation to be lost. In other words, this plot is conditional upon mutations being lost; it implies nothing about the likelihood of loss.

The fixation time plot, on the right, similarly shows the distribution of fixation times, in generations, for each of the four mutation types (conditional, similarly, upon the mutations having fixed).

8.4 Population fitness over time

The next graph we will examine is “Graph Fitness ~ Time”. At the end of a run of this recipe, it might look something like this:



This plot shows the fitness of the population over time. More specifically it shows mean absolute fitness, and (following the SLiM engine) it rescales whenever a mutation fixes, dropping the fixed mutation from the calculation. Without that rescaling, the plot would be nearly a monotonically rising curve; with the rescaling, a drop in the curve occurs each time that a beneficial mutation fixes (shown in blue). In fact neutral and deleterious mutations that fix are also shown with a blue line in this plot, but since, in this model, they almost always fix at the same time as a beneficial mutation, there are only a few fixation events in the plot that do not correspond to a drop in mean fitness due to a rescaling.

A few things can be observed in this plot. First of all, a bunch of mutations fixed over `10000` generations; the probability of beneficial mutations is probably much higher than the typical empirical rate. For the same reason, the strong-selection-weak-mutation assumption emphatically does not hold here; beneficial mutations are stacking up and competing with each other, as can be seen from both the complex wiggling of the curve in between fixation events, and from the fact that fixation events usually do not drop the mean fitness back down to `1.0` (indicating that at least one other beneficial mutation exists at intermediate frequency in the population at the same time).

We have seen the “Graph Population Visualization” plot before, and since there is no population structure in this recipe it is not interesting here; so this concludes our tour of SLiMgui’s graphing facilities. If you want to graph other things, you can of course generate an output file with the data you need, read the data into R, and generate your plots there. Also, don’t forget that you can copy SLiMgui’s graphs to the clipboard, or save them out as PDF files, using the “Copy Graph” and “Export Graph...” context menu commands.

9. Context-dependent selection using fitness() callbacks

In this and following chapters, we will show how *Eidos callbacks* can be used to modify SLiM's standard behavior. You have seen one Eidos callback already, `initialize()` callbacks that are called by SLiM at initialization time to modify the default initialization behavior (which sets up only the `SLiMSim` object). At least one `initialize()` callback in required, since SLiM's default initialization is insufficient to produce a working simulation. Other Eidos callbacks are optional, because SLiM's default behavior is sufficient. In this chapter we will look at one particular Eidos callback, the `fitness()` callback, used to modify how SLiM calculates the fitness of an individual as a function of the mutations present in this individual and potentially other simulation state.

There are just a few conceptual points to discuss before the first recipe. First of all, `fitness()` callbacks return a relative fitness value for a focal mutation in a focal individual. Neutrality is indicated by a relative fitness of `1.0`; fitness uses a different scale than selection coefficients, for which `0.0` indicates neutrality. A `fitness()` callback is called once for each mutation possessed by each individual; the callback can therefore assign a different fitness value to the same mutation depending upon the focal individual possessing the mutation. If a given individual is homozygous for a mutation, the `fitness()` callback is still called only once; a flag provided to the callback indicates whether the focal mutation is homozygous or heterozygous in the focal individual. This is because `fitness()` callbacks return a relative fitness rather than a selection coefficient: they take all of the information regarding the focal mutation in the focal individual – selection coefficient, dominance coefficient, homozygosity versus heterozygosity, genetic background, subpopulation, sex, etc. – and condense all of it into a determination of the fitness effect of the focal mutation. Each mutation in the focal individual is evaluated separately – by one or more `fitness()` callbacks if any apply, otherwise by SLiM's standard fitness equation – to produce a set of relative fitness values, one for each mutation. SLiM then multiplies these relative fitness values to determine the fitness of the individual. This process is repeated for each individual in the simulation. This is just a quick summary; see sections 19.6, 20.3, and 22.2 for a fuller explanation.

9.1 Temporally varying selection

One way to model temporally varying selection in SLiM is to use the `setSelectionCoeff()` method of `Mutation`; you can find the mutation(s) whose selection coefficient you want to change, and then use that method to make the change at a specific point in time. However, there are several disadvantages to this approach in general. First of all, the change is permanent; it would be difficult to later restore the original selection coefficient (if the modified selection regime ends, for example). Second, each mutation that you wish to modify must be changed individually. (To be fair, there are also advantages to this method; the change is done once and then is finished with, and subsequently you pay no speed penalty whatsoever for the change.)

Here we will examine another possible solution to this problem, using a `fitness()` callback:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);  // neutral
    initializeMutationType("m2", 0.5, "f", 0.1);  // beneficial
    initializeGenomicElementType("g1", c(m1,m2), c(0.995,0.005));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
2000:3999 fitness(m2) { return 1.0; }
10000 { sim.simulationFinished(); }
```

The `initialize()` callback sets up two mutation types: a very common neutral mutation type (`m1`), and an uncommon beneficial mutation type (`m2`). This produces distinctive simulation dynamics in which occasional beneficial mutations arise and sweep quickly.

However, from generation `2000` to `3999`, the simulation switches to pure neutral dynamics, because mutation type `m2` reverts to neutrality for that period of time due to the `fitness()` callback that is defined. This change in dynamics can be seen quite clearly in SLiMgui if you Recycle and then Play. Let's look at the callback in more detail:

```
2000:3999 fitness(m2) { return 1.0; }
```

The generation range used, `2000:3999`, is expressed in the usual syntax. Following that comes the declaration that this block is a `fitness()` callback, rather than an ordinary Eidos event: `fitness(m2)`. A `fitness()` callback must be declared as applying to one specific mutation type – in this case, `m2`; the callback modifies the fitness effect only of mutations belonging to that mutation type. (This is both for conceptual clarity and for efficiency.) The rest of the callback definition is a compound statement that returns a `float` value, used by SLiM as the fitness effect of the mutation. Here the value `1.0` is returned, which represents neutrality. (Remember that a neutral mutation has a selection coefficient of `0.0` but a multiplicative fitness effect of `1.0`). This is the first time we have seen the Eidos keyword `return`; it simply causes the executing script block to return immediately, passing its (optional) value out to the caller of the block, which in this case is the SLiM engine itself. It can be used in Eidos events too, although any value returned will not be used for anything.

This recipe is trivially simple, but of course the code in a `fitness()` callback can do anything, so the potential power of this mechanism should be apparent. In the context of temporally varying selection, you could make the fitness effect vary sinusoidally through time using an expression based on `sin(sim.generation)`, or make it be random in each generation with `rnorm()`, or any other effect you wish.

9.2 Spatially varying selection

The previous example showed a simple recipe implementing temporally varying selection. In this section we will see how to make selection vary spatially between subpopulations. More specifically, we will examine a model in which mutations have beneficial effects in one subpopulation, but deleterious effects in another subpopulation. Whether such mutations fix or not depends on the strength of the fitness effects, the migration rates between the subpopulations, and various other factors. The recipe:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);   // neutral
    initializeMutationType("m2", 0.5, "e", 0.1);   // deleterious in p2
    initializeGenomicElementType("g1", c(m1,m2), c(0.99,0.01));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
    sim.addSubpop("p2", 500);
    p1.setMigrationRates(p2, 0.1);   // weak migration p2 -> p1
    p2.setMigrationRates(p1, 0.5);   // strong migration p1 -> p2
}
fitness(m2, p2) { return 1/relFitness; }
10000 { sim.simulationFinished(); }
```

Here we set up two subpopulations of equal size, with weak migration from `p2` to `p1`, but with strong migration from `p1` to `p2` (remember that you can use the population visualization graph in SLiMgui to see a graphical depiction of the population structure, after you Recycle and then Step through the setup). Mutations are mostly neutral, but occasionally beneficial mutations are drawn from an exponential distribution with mean `0.1`. This is all review; the interesting part is the `fitness()` callback:

```
fitness(m2, p2) { return 1/relFitness; }
```

Here no generation range is specified; this `fitness()` callback is therefore active in every generation. Subpopulation `p2` is given as a parameter to the callback definition; this restricts the operation of the callback to only the specified subpopulation, producing spatial variation in selection. The body of the callback returns `1/relFitness` as the modified fitness effect of each `m2` mutation.

We haven't seen `relFitness` before; it is a variable defined by SLiM when a `fitness()` callback is called, and it contains the fitness value that SLiM would normally use for the mutation. By returning `1/relFitness`, we are telling SLiM to invert the normal fitness effect of all `m2` mutations in `p2`; if they are of high fitness in `p1` (`2.0`, say) they become low fitness in `p2` (`1/2.0 == 0.5`), and vice versa.

There is a point worth clarifying here. Mutation type `m2` draws selection coefficients from an exponential DFE; each mutation of type `m2` is thus unique. Because of this, the `fitness()` callback here is not called just once per generation, to calculate a modified fitness effect for all mutations of type `m2`; it is called *once per individual per `m2` mutation*, and it calculates a modified fitness effect for *that* mutation in *that* individual. These calculations can therefore depend upon both the specific mutation and the specific individual. In addition to the `relFitness` variable that contains the default relative fitness effect for the mutation, SLiM also defines `mut`, the mutation being assessed; `subpop`, the subpopulation containing the individual possessing the mutation; `homozygous`, a flag which is true if the individual is homozygous for the mutation, false otherwise; and a few others as well that we will see in the next sections. The code in a `fitness()` callback can use all of these variables to calculate its modified fitness effect.

Because `fitness()` callbacks might be called thousands or even millions of times every generation, SLiM and Eidos are highly optimized to make those calls as fast as possible. You should do your part by making your Eidos code as tight as possible; writing an inefficient `fitness()` callback is an excellent way to make your simulation slow to a crawl. See section 18.1 for some tips on how to write fast Eidos code.

If you paste this recipe into SLiMgui, Recycle, and Play, you will see the spatial dynamics very clearly; mutations will spread that are beneficial in `p1`, turning that subpopulation's individuals green, but deleterious in `p2`, turning that subpopulation's individuals red. With the recipe as written, these mutations will often fix; the strong migration from `p1` versus the weak migration from `p2` gives `p1` an advantage, allowing it to force `p2` to fix mutations that are deleterious in that context. If you reverse the migration bias, that will no longer happen; instead `p2` will be able to force `p1` to lose mutations that are beneficial in that context. One could easily use this model to explore this scenario in detail, with questions such as the effect of subpopulation size, migration rate, selection strength, and so forth. Since neutral mutations are also in the model, one could also ask questions about how these sorts of dynamics affect neutral diversity and divergence. Not bad for sixteen lines of code!

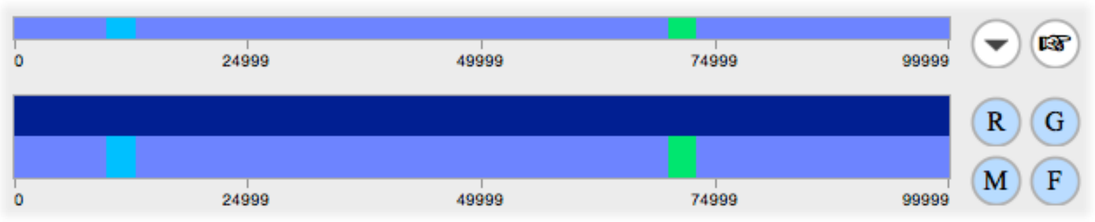
9.3 Fitness as a function of genomic background

9.3.1 Epistasis

The `fitness()` callback mechanism can also make the fitness effect of a mutation depend upon the genetic background of the individual that possesses the mutation. One example of this is epistasis, in which two loci interact to produce a non-additive fitness effect (Philipps 2008). The recipe here is a bit contrived – a more realistic model would probably use introduced epistatic mutations rather than random mutations – but it serves to illustrate the concept:

```
initialize() {
    initializeMutationRate(1e-8);
    initializeMutationType("m1", 0.5, "f", 0.0);  // neutral
    initializeMutationType("m2", 0.5, "f", 0.1);  // epistatic mut 1
    initializeMutationType("m3", 0.5, "f", 0.1);  // epistatic mut 2
    initializeGenomicElementType("g1", m1, 1);
    initializeGenomicElementType("g2", m2, 1);    // epistatic locus 1
    initializeGenomicElementType("g3", m3, 1);    // epistatic locus 2
    initializeGenomicElement(g1, 0, 10000);
    initializeGenomicElement(g2, 10001, 13000);
    initializeGenomicElement(g1, 13001, 70000);
    initializeGenomicElement(g3, 70001, 73000);
    initializeGenomicElement(g1, 73001, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
10000 { sim.simulationFinished(); }
fitness(m3) {
    if (genome1.countOfMutationsOfType(m2))
       return 0.5;
    else if (genome2.countOfMutationsOfType(m2))
       return 0.5;
    else
       return relFitness;
}
```

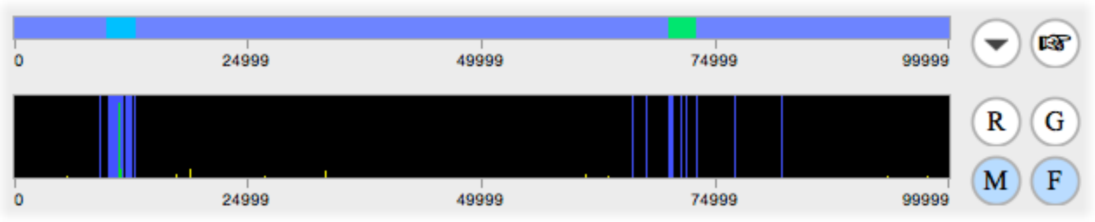
The `initialize()` callback sets the stage by making three mutation types, three genomic element types, and five genomic elements. Over the majority of the chromosome, genomic element type `g1` is used; it generates only neutral mutations. In a locus spanning `10001:13000`, genomic element type `g2` is used, which generates mutations of type `m2`, which are beneficial with a selection coefficient of `0.1`. In a second locus spanning `70001:73000`, genomic element type `g3` is used, which generates mutations of type `m3`, which are also beneficial. If you turn on display of genomic elements in SLiMgui, the resulting setup looks like this:



The twist, however, comes in the `fitness()` callback, which makes mutations of types `m2` and `m3` interact epistatically. Any mutation of type `m3` has a fitness effect of `0.5` – strongly deleterious – if it is found in the same genome as any mutation of type `m2`. This is achieved in several steps. First of all, `genome1` and `genome2` are defined by SLiM for `fitness()` callbacks; they are the two genomes (the two homologous chromosomes) of the individual carrying the mutation that is being evaluated. The call `genome1.countOfMutationsOfType()` method counts the mutations of type `m2` in the first genome; if that count is non-zero, the `if` statement evaluates it as true (`T`), and `0.5` is returned, making the focal mutation deleterious. The next two lines perform the same check for `genome2` (these two `if` conditions could be combined into a single test using the "`logical` or" operator, `|`, but the line of code would then be too long to fit without wrapping here). If neither `Genome` object contains a mutation of type `m2`, the final `else` clause will execute and `relFitness` will be returned, keeping the normal fitness effect of the focal mutation without modification. There are some new concepts here, and this manual is not going to explain them all in detail; for full discussions of the `logical` type, the behavior of true and false values in Eidos, and so forth, please refer to the Eidos manual, which explains these ideas thoroughly.

Note that mutations of type `m2` suffer no fitness penalty from sharing an individual with an `m3` mutation; the `fitness()` callback affects only `m3` mutations. Since the fitness of the carrying individual will be severely compromised, however, the net effect is that `m2` and `m3` mutations are rarely found together; collocation effectively harms `m2` mutations just as much as `m3` mutations.

This produces some interesting dynamics. Type `m2` and `m3` mutations arise fairly often, and quickly sweep to fixation; however, they never sweep together, so if a mutation at one of the two epistatic loci is sweeping, the other locus will have no active mutations. The two loci thus "take turns" sweeping new mutations to fixation. Since new beneficial loci sweep so often, neutral loci generally fix only if they are linked to a beneficial mutation. Because of recombination, that is most likely to happen close to one of the two epistatic loci, so if we run the full simulation and then turn on display of fixed mutations, we see a pattern of clustering near the epistatic loci:



All of the fixed mutations within the loci are beneficial epistatic mutations, since the two loci generate only those mutation types. All of the bands for fixed mutations outside of those loci, however, are for neutral mutations that hitchhiked.

The astute reader will have noticed a problem with all this. Biologically, this dynamic of "taking turns" sweeping at one or the other locus makes no sense. If a mutation of type `m2` sweeps to fixation at the `g2` locus, that mutation still exists in the genome, and the epistatic interaction between `m2` and `m3` mutations should prevent an `m3` mutation from sweeping, forever after. That objection is correct, and points out a very important issue.

The reason that this recipe behaves in this manner has to do with the way that SLiM handles fixed mutations (see section 19.3). When a mutation fixes, SLiM normally removes it from the simulation, replacing it with a `Substitution` object that provides a permanent record of the fixed mutation. The assumption is that since every individual possesses the fixed mutation, it has the same fitness effect in every individual, and therefore can be ignored. However, epistasis violates that assumption, since the fixed mutation causes a differential fitness effect among individuals based upon the genetic background in which it is found. SLiM's replacement of fixed `m2` and `m3` mutations in this model thus produces incorrect behavior that does not accurately model epistasis.

What to do? Happily, SLiM provides a way to handle this situation. The `MutationType` class has a `logical` property named `convertToSubstitution`; by default it is `T`, indicating to SLiM that fixed mutations of that type should be replaced by `Substitution` objects. We can set it to `F` instead, telling SLiM to keep all mutations of that type active in the simulation even once fixed. (See sections 18.3 and 20.9.1 for further discussion of this property). The new recipe:

```
initialize() {
    initializeMutationRate(1e-8);
    initializeMutationType("m1", 0.5, "f", 0.0);  // neutral
    initializeMutationType("m2", 0.5, "f", 0.1);  // epistatic mut 1
    m2.convertToSubstitution = F;
    initializeMutationType("m3", 0.5, "f", 0.1);  // epistatic mut 2
    m3.convertToSubstitution = F;
    initializeGenomicElementType("g1", m1, 1);
    initializeGenomicElementType("g2", m2, 1);    // epistatic locus 1
    initializeGenomicElementType("g3", m3, 1);    // epistatic locus 2
    initializeGenomicElement(g1, 0, 10000);
    initializeGenomicElement(g2, 10001, 13000);
    initializeGenomicElement(g1, 13001, 70000);
    initializeGenomicElement(g3, 70001, 73000);
    initializeGenomicElement(g1, 73001, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
10000 { sim.simulationFinished(); }
fitness(m3) {
    if (genome1.countOfMutationsOfType(m2))
      return 0.5;
    else if (genome2.countOfMutationsOfType(m2))
      return 0.5;
    else
      return relFitness;
}
```

This will now produce the correct epistatic dynamics. If you run this model in SLiMgui, you will see that one or the other epistatic locus wins an initial contest by fixing a mutation. Once that happens, the other locus will never manage to establish.

The `convertToSubstitution` property should be used to prevent fixed mutation substitution whenever the assumption of equal effects in all individuals would be violated, whether by a `fitness()` callback introducing a mechanism like epistasis, or by differential effects of the mutation type on mate choice or other dynamics. SLiM is not able to guess when substitution should be turned off, so you must keep this caveat in mind. However, also keep in mind that turning off substitution will make your models run much more slowly.

9.3.2 Polygenic selection

Another way in which the fitness effect of one mutation can depend upon the genetic background is polygenic selection. As in epistasis, multiple mutations collocated in a single individual produce a non-additive effect; but whereas epistasis produces an effect on mutations at locus A based upon the simple presence or absence of mutations at locus B, polygenic selection produces an overall fitness effect that depends upon *how many* mutations of a given type exist.

That description contrasts the concept of polygenic selection with epistasis, but technically, it really is a type of epistasis; the genetic background against which a given mutation is found influences the fitness effect of that mutation. Given this, we will need to use the `convertToSubstitution` property of `MutationType` to suppress the substitution of the epistatic mutations, as in the previous example, so that even after they fix they continue to be taken into account by the fitness calculations of the model.

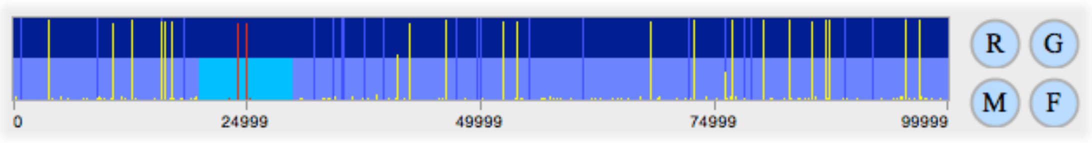
Here is a recipe for a simple polygenic selection scenario:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);    // neutral
    initializeMutationType("m2", 0.5, "f", -0.04);  // polygenic
    m2.convertToSubstitution = F;
    initializeGenomicElementType("g1", m1, 1);
    initializeGenomicElementType("g2", m2, 1);
    initializeGenomicElement(g1, 0, 20000);
    initializeGenomicElement(g2, 20001, 30000);
    initializeGenomicElement(g1, 30001, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
1:10000 {
    if (sim.mutationsOfType(m2).size() > 100)
      sim.simulationFinished();
}
fitness(m2) {
    count = sum(c(genome1,genome2).countOfMutationsOfType(m2));
    if ((count > 2) & homozygous)
      return 1.0 + count * 0.1;
    else
      return relFitness;
}
```

The `initialize()` callback here sets up a chromosome with a genomic element of type `g2` in a central locus, generating mutations of mutation type `m2` that are under polygenic selection; the rest of the chromosome uses `g1` and `m1`, generating neutral mutations.

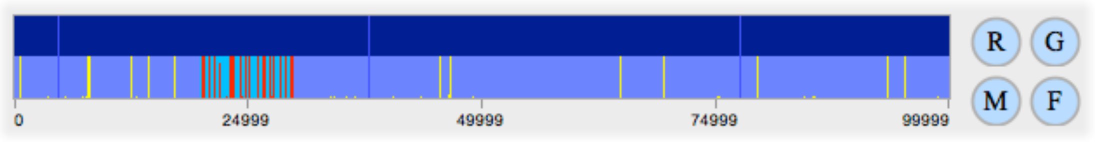
The `fitness()` callback, defined on mutation type `m2`, sets up the conditions for polygenic selection. First it counts the total number of mutations of type `m2` on both chromosomes of the focal individual, using the `countOfMutationsOfType()` method we saw in the previous section, and assigns that value to `count`. It does it in a slightly odd way; it first creates an `object` vector containing both genomes, with `c(genome1,genome2)`, then calls `countOfMutationsOfType()` on that vector to produce a result vector containing two `integer` values (the counts for `genome1` and `genome2`, respectively), and then uses `sum()` to add the two values together to get an overall count. (You can read more about the mechanics of how this works in the Eidos manual, as usual.) Then, if `count` is greater than 2 and the focal mutation is homozygous in the focal individual (using the flag `homozygous` that is set by SLiM for `fitness()` callbacks), a beneficial fitness effect is returned by `1.0 + count * 0.1` (where the `1.0` provides a baseline of neutrality). Otherwise, `relFitness` is returned so that the normal (deleterious) fitness effect of the mutation is unchanged.

Running this recipe in SLiMgui shows the expected dynamics: within the locus where polygenic selection is active, pairs (or more) of mutations drive to fixation simultaneously, because single mutations on their own are deleterious. Many deleterious mutations flicker in and out of existence in that locus; when, by chance, one manages to become both homozygous and collocated with another mutation within the locus, the combination is favorable and they fix together:



Once one pair of these mutations has fixed, all individuals possess a homozygous mutation (two, in fact) in their genetic background, and so the requirements for further mutations to be beneficial are greatly relaxed. Individual mutations are then immediately beneficial, through their epistatic effect on the fixed mutations, even though their own fitness effect will remain deleterious until they become homozygous.

Incidentally, the use of `homozygous` in the `fitness()` callback here may seem strange; a mutation only gets the polygenic selection bump-up if it is homozygous in the focal individual. This is a quick hack to prevent a particular type of dynamics from taking over, in which mutations of type `m2` are prevented from going to fixation because recombination is suppressed. Recombination gets suppressed because it would break apart linked collections of mutations that are presently benefiting from the polygenic selection. Without the `homozygous` requirement, the highest possible fitness for an individual comes from having completely different sets of mutations in its two genomes; fixation is therefore blocked. If you delete the "`& homozygous`" check from the recipe, you can see the effect of this in SLiMgui:



As in the previous section, models involving polygenic selection in SLiM are likely to involve introduced mutations, and might thus avoid this issue.

See sections 13.1 and 13.10 for more sophisticated recipes that construct a quantitative trait based upon the additive effects of multiple loci.

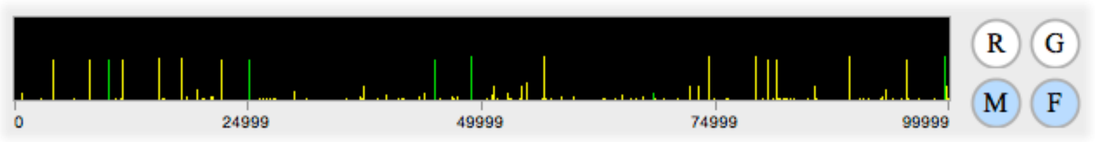
9.4 Fitness as a function of population composition

9.4.1 Frequency-dependent selection

In previous sections we have seen how we can use a `fitness()` callback to modify the fitness effects of mutations in order to model scenarios such as epistasis, polygenic selection, and spatiotemporal variation in selection. Now we will shift to making the fitness of mutations be a function of population composition. First we'll look at frequency-dependent selection, in which the fitness effect of a mutation depends upon the frequency of the mutation in the population (Ayala & Campbell 1974). Let's start with a simple recipe for negative frequency-dependence:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);    // neutral
    initializeMutationType("m2", 0.5, "f", 0.1);    // balanced
    initializeGenomicElementType("g1", c(m1,m2), c(999,1));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
10000 { sim.simulationFinished(); }
fitness(m2) {
    return 1.5 - sim.mutationFrequencies(p1, mut);
}
```

The idea here should be pretty clear; if the `mutationFrequencies()` method tells us that `mut` is rare in `p1`, then the mutation will be highly beneficial, but if it tells us that `mut` is common, the mutation will be deleterious. These dynamics prevent the mutation from either fixing or being lost; instead we have what is called "balancing selection", in which selection favors keeping mutations of that type at an intermediate frequency. (See section 9.5 for an adaptation of this recipe using `setSelectionCoeff()` instead; and see section 11.3 for a very different model of balancing selection, using a `modifyChild()` callback instead of a `fitness()` callback.) Running this for a while in SLiMgui gives us a picture something like this (where the yellow lines are neutral mutations and the green lines are the mutations under balancing selection):



There are five `m2` mutations under balancing selection, all at frequency ~`0.5` since that is the point at which the fitness effect changes from beneficial to deleterious according to the callback.

Next let's look at a model of positive frequency-dependence:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);    // neutral
    initializeMutationType("m2", 0.5, "f", 0.1);    // positive freq. dep.
    initializeGenomicElementType("g1", c(m1,m2), c(999,1));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
10000 { sim.simulationFinished(); }
fitness(m2) {
    return 1.0 + sim.mutationFrequencies(p1, mut);
}
```

The way this works is probably pretty obvious at this point; at low frequencies (as calculated by `mutationFrequencies()`) mutations of type `m2` are close to neutral, but at higher frequencies they become strongly beneficial. Note that these mutations still do not sweep to fixation as quickly as one might expect. This is because `fitness()` callbacks get called only once per mutation *per individual*. If an individual carries one copy of a mutation (i.e., is a heterozygote), the `fitness()` callback is called once. If an individual carries two copies (i.e., is a homozygote), the `fitness()` callback is *still* called only once. Thus, if a `fitness()` callback does not explicitly consult the `homozygous` flag, as described in sections 9.3.2 and 21.2, it will produce an effect of complete dominance, regardless of the original dominance coefficient set in the mutation type, thereby hindering fixation. If you wish to model codominance in the above scenario, just include the `homozygous` flag in your calculations. In this case, we could alter our recipe in the following way:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);    // neutral
    initializeMutationType("m2", 0.5, "f", 0.1);    // positive freq. dep.
    initializeGenomicElementType("g1", c(m1,m2), c(999,1));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
10000 { sim.simulationFinished(); }
fitness(m2) {
    dominance = asInteger(homozygous) * 0.5 + 0.5;
    return 1.0 + sim.mutationFrequencies(p1, mut) * dominance;
}
```

9.4.2 Kin selection and inclusive fitness

According to the theory of kin selection and inclusive fitness (Hamilton 1964ab; Dawkins 1976), a mutation that promotes altruism towards kin can spread even if its direct fitness effect on individuals is negative (because they are devoting energy to behaving altruistically towards related individuals), if the mutation has indirect benefits (in the form of related individuals behaving altruistically towards carriers of the mutation). In other words, one cannot look at things solely from the perspective of the individual; one must look from the perspective of the gene, and see whether the indirect benefits that accrue to carriers of that gene outweigh the direct costs of possessing the gene.

This is a little tricky to model directly in SLiM, since all fitness calculations are done from the perspective of the individual, and since there is no phase of the life cycle in which individuals interact socially to affect survival probabilities, etc. This kin selection model will therefore look a bit tautological, because the fitness calculation for an individual just tots up to a net benefit: the indirect benefit outweighs the direct cost. (But see section 9.4.4 for a much more satisfying approach.) Nevertheless, we can cook up a recipe that shows the concept by using mutations at two different loci to serve as the two halves of the inclusive fitness equation:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);    // neutral
    initializeMutationType("m2", 0.5, "f", 0.1);    // kin recognition
    m2.convertToSubstitution = F;
    initializeMutationType("m3", 0.5, "f", 0.1);    // kin benefit
    m3.convertToSubstitution = F;
    initializeGenomicElementType("g1", m1, 1);
    initializeGenomicElementType("g2", m2, 1);
    initializeGenomicElementType("g3", m3, 1);
    initializeGenomicElement(g1, 0, 10000);
    initializeGenomicElement(g2, 10001, 13000);
    initializeGenomicElement(g1, 13001, 70000);
    initializeGenomicElement(g3, 70001, 73000);
    initializeGenomicElement(g1, 73001, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
3000 { sim.simulationFinished(); }
fitness(m2) {
    // count our kin and suffer a fitness cost for altruism
    dominance = asInteger(homozygous) * 0.5 + 0.5;
    return 1.0 - sim.mutationFrequencies(p1, mut) * dominance * 0.1;
}
fitness(m3) {
    // count our kin and gain a fitness benefit from them
    m2Muts = individual.uniqueMutationsOfType(m2);
    kinCount = sum(sim.mutationFrequencies(p1, m2Muts));
    return 1.0 + sim.mutationFrequencies(p1, mut) * kinCount;
}
```

Here we have a locus spanning `10001:13000` that contains mutations governing kin recognition (using mutation type `m2` in genomic element type `g2`), and a locus spanning `70001:73000` with mutations which reap a benefit from having kin (using mutation type `m3` in genomic element type `g3`). Mutations at the `m2` locus are always deleterious; their fitness effect decreases from `1.0`, growing smaller as they become more common (negative frequency-dependence, but without a positive fitness effect even at low frequency). This locus represents a facility for kin recognition and costly altruistic behavior towards kin. By itself, m2 mutations would almost invariably die out.

However, mutations at the m3 locus represent the target of altruism from kin. The fitness() callback here computes a metric based upon how many other individuals share the focal individual's mutations at the kin-recognition locus. Carriers of mutations at the m3 locus (a locus that attracts altruistic behavior from kin) benefit from these interactions based upon the magnitude of shared kinship.

If you run this model in SLiMgui, you can see that mutations at the m2 locus sometimes fix, despite the fact that the direct fitness benefit of those mutations is negative. This does not happen in isolation; instead, a mutation at the kin recognition locus will rise to fixation at the same time that an mutation at the benefit locus rises, and the mutation at the benefit locus needs to initiate the process. Together, however, the mutations at the two loci can rise to fixation.

This model is somewhat unsatisfying from an individual-based perspective – one would like to see individual interactions in which the altruistic individual suffers without benefit, while the kin individual gains without cost (see section 9.4.4 for such a recipe) – but the fitness() callback equations in this recipe essentially encapsulate such interactions on an aggregated level. If you consider the effects of kin recognition and altruism to be composed of many small acts that can be averaged over the lifetime of an individual – as is likely to be the case in most empirical systems involving kin selection – then this approach is actually quite reasonable.

9.4.3 Cultural effects on fitness

Sometimes fitness might be influenced by environmental factors as well as genetic factors. In some cases, these environmental factors would be associated with the subpopulation in which an individual resides; in that case, they can be modeled as spatial variation in selection (see section 9.2). In other cases, however, the environmental factors might be a matter of individual variation that is not correlated with the subpopulation; that possibility is what we will explore in this recipe.

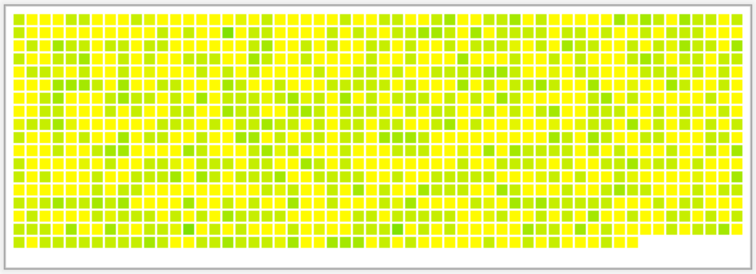
In particular, we will make a simple model of cultural differences between individuals. Each individual will be assigned to one of two cultural groups at birth. If an individual belongs to one cultural group, a particular type of mutation will be beneficial; if the individual belongs to the other cultural group, those mutations will be neutral. An analogue to this in human history, which we will loosely follow here, would be the allele conferring the ability to digest lactose as an adult; if an individual belongs to a cultural group that drinks milk in adulthood, mutations promoting the retention of the lactase enzyme into adulthood are beneficial, whereas if the individual belongs to a cultural group that does not drink milk in adulthood, such mutations are nearly neutral (or perhaps slightly deleterious, due to the energetic investment of producing an unneeded enzyme).

For the initial version of this model, the cultural group into which an individual is assigned will be entirely random. The cultural group of an individual will be tracked using the tag property of Individual, an integer property that is not used at all by SLiM, and is thus free for you to use as you wish. We will use a tag value of 1 to indicate a milk-drinker, and a value of 0 to indicate a non-milk-drinker. The tag value will be set up in a late() event that runs after offspring are generated but before fitness values are calculated. The recipe:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);   // neutral
    initializeMutationType("m2", 0.5, "f", 0.1);   // lactase-promoting
    m2.convertToSubstitution = F;
    initializeGenomicElementType("g1", c(m1,m2), c(0.99,0.01));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
```

```
1 { sim.addSubpop("p1", 1000); }
10000 { sim.simulationFinished(); }
late() {
    // Assign a cultural group: milk-drinker == 1, non-milk-drinker == 0
    p1.individuals.tag = rbinom(1000, 1, 0.5);
}
fitness(m2) {
    if (individual.tag == 0)
       return 1.0;         // neutral for non-milk-drinkers
    else
       return relFitness;  // beneficial for milk-drinkers
}
```

When run, the occasional mutations of type `m2` sweep to fixation, as you might expect, but even when they are close to fixation only about half of the population – the milk-drinkers – are experiencing a fitness benefit from the mutation. This can be seen easily in the pattern of individual fitness values displayed in SLiMgui when an `m2` mutation was at a frequency of `0.95`:



The `m2` mutations are prevented from being removed at fixation, by setting the `convertToSubstitution` property of `m2` to `F`. As the model runs, `m2` mutations accumulate, and the fitness benefits of being a milk-drinker become larger and larger. Since that status is assigned randomly, however, this does not affect the frequency of milk-drinking; a randomly chosen half of the population is less likely to pass on its genes to the next generation, but milk-drinking remains a random choice.

The `late()` event assigns cultural `tag` values to all of the individuals in the new offspring generation. We first generate `1000` random values, either `0` or `1`, using `rbinom()` to draw from a simple binomial distribution. The resulting vector is assigned directly into `p1.individuals.tag` using the multiplexed assignment semantics of Eidos to put each value in the vector into the `tag` property of the corresponding individual in subpopulation `p1` (see the Eidos manual for further discussion of multiplexed assignment).

Given those `tag` values, the `fitness()` callback is then trivial: for the lactase-promoting mutations of type `m2`, the fitness is neutral if the `tag` value of a given individual carrying the mutation is `0`, indicating a non-milk-drinker, whereas for milk-drinkers, with a `tag` value of `1`, `relFitness` is returned to accept SLiM's default calculated fitness for the mutation (which uses both the selection coefficient of `0.1` and the dominance coefficient of `0.5` defined for `m2`). This could be modified to make the mutations slightly deleterious in non-milk-drinkers, if one wished, of course.

In this model, the cultural group of an individual is assigned randomly. In many cases one would wish this trait to have some degree of heritability, even though it is not genetically based; in humans and some other species, individuals inherit their culture from their parents through social learning. To implement that, a `modifyChild()` callback is needed; we will therefore take this model up again in section 12.1.

9.4.4 The green-beard effect

The recipe in section 9.4.2 modeled kin-selection effects by averaging the beneficial and deleterious effects of altruistic acts across the whole population. That was unsatisfying, because it looked somewhat tautological; each individual received an average benefit from the existence of kin in the population (directing altruistic acts toward the individual), and each individual received an average harm from the existence of kin (by committing costly altruistic acts), and if the average benefit outweighed the average harm, kin-directed altruism spread because the net effect on every individual was beneficial. In a large population, with many small altruistic acts occurring between all kin, that model is actually quite reasonable; but it leaves open the question of whether inclusive fitness theory is really correct that kin-directed altruism can evolve even when the individuals committing the altruistic acts (at a cost to themselves) do not necessarily receive a benefit from altruistic acts by others. In a more individual-oriented model that doesn't average the benefits and costs across the whole population, does kin-directed altruism still evolve? Using the `tag` property of the `Individual` class, as shown in the previous section, we can develop a model to answer that question.

Here we will explore this question in a closely related evolutionary problem, the modeling of *green-beard alleles* (Hamilton 1964ab; Dawkins 1976). A green-beard allele causes three pleiotropic effects: (1) a phenotypic trait of some kind (the "green beard"), (2) the ability to recognize other individuals possessing this phenotypic trait, and (3) a tendency to direct altruistic acts toward other individuals possessing this phenotypic trait (at some cost to the altruistic individual, and some benefit to the receiving individual).

The idea for this recipe is to, in effect, add a new stage to the generation life cycle. In this new life cycle stage, a finite number of one-on-one interactions between randomly chosen individuals in the population are modeled. If the individuals both have the green-beard allele, an altruistic act occurs and one receives a benefit and the other receives a cost; if either individual does not have the green-beard allele, no altruistic act occurs and the interaction is neutral. The benefits and costs incurred by each individual are tallied up separately, and are taken into account in a `fitness()` callback that models the fitness effect of the green-beard allele for each individual based upon its particular interaction tally. Some individuals with the green-beard allele will, by chance, incur nothing but costs from their interactions, harming themselves to the point where they are unlikely to reproduce. Other individuals with the green-beard allele will, by chance, incur a mixture of costs and benefits, or if they're lucky, nothing but benefits; their outcome will thus be neutral or positive.

Let's get to the recipe. We'll build it one step at a time; the first step is just to set up a single subpopulation with two mutation types:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);     // neutral
    initializeMutationType("m2", 0.5, "f", -0.01);   // green-beard
    m2.convertToSubstitution = F;
    initializeGenomicElementType("g1", m1, 1);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
fitness(m2) { return 1.0; }  // neutral
10000 { sim.simulationFinished(); }
```

Mutation type `m2` will be used for green-beard alleles, but is not used yet. It is set to not convert into a `Substitution` object upon fixation, using the `convertToSubstitution` property of

MutationType, so that we can easily see whether or not it has fixed at the end of a model run. Its selection coefficient of -0.01 is just to give it a distinctive color in SLiMgui; the green-beard allele is neutral here, because the fitness() callback gives a relative fitness of 1.0 for the allele, overriding selection coefficient of the mutation type. And in any case m2 is not used yet; as it stands, then, this is just a model of neutral drift using only m1.

Now let's add a system for tagging individuals with costs and benefits, replacing the fitness() callback in the code above:

```
1: late() {
    p1.individuals.tag = 0;
}
fitness(m2) { return 1.0 + individual.tag / 10; }
```

Every individual in SLiM has a tag property that can be set to any value. As explained in the previous section, the tag field is not used by SLiM; it's just scratch space for models to use as they please. In this recipe, we use it to hold the cost/benefit tallies for individuals. The fitness() callback then adds the tag value for the individual it is evaluating to a neutral relative fitness of 1.0. The tag value is an integer, so we divide it by 10 in the callback; each increment or decrement of an individual's tag will represent a change to its relative fitness of 0.1 or -0.1.

Let's introduce a green-beard allele into the population. It won't be very interesting if it just gets lost due to drift in the first generation or two, at green-beard alleles at low frequency generally drift freely since interactions between the rare green-beards are unlikely – so we'll introduce several copies of it to give it an initial boost. The concept of introducing a mutation is covered in depth in section 10.1, but it should be pretty clear what's going on here:

```
1 late() {
    target = sample(p1.genomes, 100);
    target.addNewDrawnMutation(m2, 10000);
}
```

This code draws 100 target genomes from the population using the sample() function (which samples without replacement, by default). It then adds a new mutation of type m2 to those target genomes with a single call to addNewDrawnMutation(). This call adds the same new mutation to all of the target genomes, rather than a different new mutation to each genome, because the addNewDrawnMutation() method is a class method of Genome, not an instance method, and it is therefore called just once, rather than being multicast out to each instance. This is conceptually similar to writing a static member function in C++ (which is like a class method in Eidos) to perform an operation across a vector of objects. That static member function would take a vector of objects as one of its parameters; in Eidos, you instead call the class method on the target vector, as seen here, just like calling an instance method. If this is not clear, don't worry; it is not an essential point, since the syntax for calling class methods and instance methods is identical in Eidos. You can consult the Eidos manual for more details on class versus instance methods.

Some individuals might receive two copies of the green-beard mutation (one in each of their genomes), and end up being homozygous, but there is no harm in that, and most of the individuals targeted by this code will end up heterozygous for the new green-beard allele. (You could guarantee heterozygosity by sampling individuals instead of genomes, and then getting just one genome from each sampled individual; conversely, you could guarantee homozygosity by sampling individuals and then adding to both of the genomes of each sampled individual.) Again, it should be emphasized that adding 100 copies is in no way "cheating"; this is just a model of whether a green-beard allele can rise from low frequency to fixation, rather than a model of whether a single copy of a green-beard allele can rise all the way to fixation. It would be easy to construct the latter model in SLiM using the tools introduced in section 10.2.

Now we need to make our green-beards interact! We'll do this with an extension to our previous `1:` event:

```
1: late() {
    p1.individuals.tag = 0;

    for (rep in 1:50) {
        individuals = sample(p1.individuals, 2);
        i0 = individuals[0];
        i1 = individuals[1];
        i0greenbeards = i0.countOfMutationsOfType(m2);
        i1greenbeards = i1.countOfMutationsOfType(m2);

        if (i0greenbeards & i1greenbeards) {
            alleleSum = i0greenbeards + i1greenbeards;
            i0.tag = i0.tag - alleleSum;        // cost to i0
            i1.tag = i1.tag + alleleSum * 2;    // benefit to i1
        }
    }
}
```

This bears some explaining. First, we zero out all of the individual `tag` values, as before. Then we run a loop `50` times, to produce `50` interactions between pairs of individuals (which might or might not possess green beards). Each time through the loop, we draw two individuals from the population using `sample()`, giving us a vector `individuals` containing two objects of class `Individual` which we extract into `i0` and `i1`.

The next two lines count the number of `m2` mutations contained in the two genomes belonging to each individual. The value of `i0greenbeards` and `i1greenbeards`, then, is `0` if the corresponding individual does not have the green-beard mutation at all, `1` if it is heterozygous, or `2` if it is homozygous. This is equivalent to, but more concise than, writing:

```
i0greenbeards = i0.genomes[0].countOfMutationsOfType(m2)
                    + i0.genomes[1].countOfMutationsOfType(m2);
```

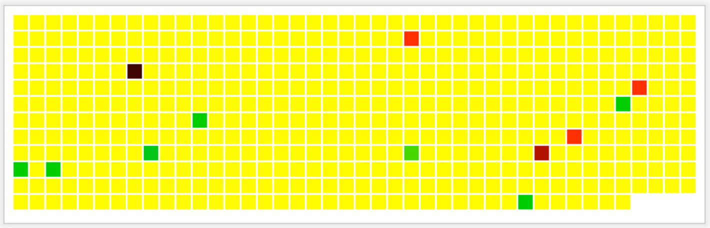
(and the same for `i1greenbeards`).

Next comes an `if` statement that will execute if both `i0greenbeards` and `i1greenbeards` are non-zero (since in Eidos, as in many languages, `0` is considered false and any non-`0` value is considered true). So this executes if and only if both of the interacting individuals are at least heterozygous for the green-beard allele. In that case, `alleleSum` is computed as the total number of green-beard alleles between the two individuals; this makes the green-beard effect stronger when homozygotes are involved, weaker when heterozygotes are involved. Finally, the `tag` values of the two interacting individuals are modified to reflect the interaction; individual `i0` acts altruistically and incurs a cost, whereas individual `i1` receives the altruistic act and gets a benefit. The costs and benefits are added to the `tag` value of each individual. Note that the benefit is larger than the cost; this makes the average fitness effect of the green-beard allele positive, and thus means that the green-beard allele is selected for, on average, in each generation. But as promised, the benefit and the cost are incurred by different individuals in this model. Indeed, the altruistic individual feels a nearly lethal fitness effect, if both interacting individuals are homozygous. From the perspective of the individual, it is a truly selfless altruistic sacrifice. From the perspective of the green-beard allele, it is an entirely selfish act, however – which is why the "selfish gene" perspective has so much explanatory power.

For the record, here is the full recipe for our green-beard model:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);     // neutral
    initializeMutationType("m2", 0.5, "f", -0.01);   // green-beard
    m2.convertToSubstitution = F;
    initializeGenomicElementType("g1", m1, 1);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
1 late() {
    target = sample(p1.genomes, 100);
    target.addNewDrawnMutation(m2, 10000);
}
1: late() {
    p1.individuals.tag = 0;
    
    for (rep in 1:50) {
       individuals = sample(p1.individuals, 2);
       i0 = individuals[0];
       i1 = individuals[1];
       i0greenbeards = i0.countOfMutationsOfType(m2);
       i1greenbeards = i1.countOfMutationsOfType(m2);
       
       if (i0greenbeards & i1greenbeards) {
          alleleSum = i0greenbeards + i1greenbeards;
          i0.tag = i0.tag - alleleSum;       // cost to i0
          i1.tag = i1.tag + alleleSum * 2;   // benefit to i1
       }
    }
}
fitness(m2) { return 1.0 + individual.tag / 10; }
10000 { sim.simulationFinished(); }
```

If you Recycle and run this recipe in SLiMgui, it may take several tries before the green-beard mutation "catches" and rises to fixation. Again, this is because its fitness effect is close to neutral when it is at low frequency; early on, it is quite liable to be lost simply due to drift. Once the mutation "catches", though, the population view will show something like this:



This display, of the model when the green-beard allele is at a frequency of around 0.3, shows the result of the individual interactions between green-beards. Some benefit from those interactions, and are colored in a shade of green or blue (depending on the magnitude of the benefit); some are harmed, and are colored in a shade of orange or red, shading down to black (depending on the magnitude of the harm).

Even once the green-beard mutation has fixed, the majority of individuals will be yellow (indicating neutrality – a relative fitness of exactly `1.0`), because only `50` pairs of individuals are chosen to interact in each generation. The larger the number of interactions, relative to the population size, the stronger the selection will be in favor of the green-beard allele. If you increase the number of interactions from `50` to `5000`, for example, there will be so many interactions relative to the population size that the green-beard allele will rise to fixation almost deterministically. In this case, this recipe has approached almost to the realm of the section 9.4.2's recipe, where computing averaged effects across the whole population was used to model the behavior of the system. With only `50` interactions, however, the model is quite stochastic in its behavior, and the green-beard allele will sometimes be lost even when it has risen as high as a frequency of `0.5`.

This recipe is, from a rather sidelong angle, basically a model of a selective sweep, and as such, it showed how to introduce a new mutation into a population and watch it sweep to fixation. In the next chapter, that subject will be treated comprehensively.

9.5 Changing selection coefficients with `setSelectionCoeff()`

The preceding recipes have demonstrated the use of `fitness()` callbacks to implement a wide variety of different types of selection in SLiM. It is worth noting, however, that it is also possible to simply change the selection coefficient of a mutation using the `setSelectionCoeff()` method of `Mutation` (see section 21.8.2). Indeed, this can have large performance advantages, since executing Eidos callbacks is relatively slow. However, this strategy can only be applied in very limited cases.

First of all, if you want the fitness effect of a mutation to vary from individual to individual – whether because of the genetic background of the individual, or the subpopulation the individual is in, or any other individual-specific model state – then a `fitness()` callback is necessary. This is because changing the selection coefficient of a mutation using `setSelectionCoeff()` changes that mutation's selection coefficient for all individuals, in all subpopulations. The recipes in sections 9.2 (spatially varying selection) and 9.3 (genomic background effects) could therefore not be implemented using `setSelectionCoeff()`, nor could those of sections 9.4.3 (cultural effects on fitness) or 9.4.4 (green-beard alleles).

Second, if you want a fitness effect to be temporary then it is often best to use a `fitness()` callback, because when the callback is no longer active mutations will automatically revert to their original effect. To take the recipe in section 9.1 (temporally varying selection) as an example, when the callback expires the `m2` mutations revert back to their original selection coefficient of `0.1` without needing to be re-set to `0.1`; indeed, their selection coefficients are `0.1` the entire time, the `fitness()` callback just overrides that with its own effect. If this recipe used `setSelectionCoeff()` instead, the original selection coefficients would need to be restored when the altered fitness regime expired. In this case that would be straightforward – just set them all to `0.1` with another call to `setSelectionCoeff()` – but if the `m2` mutations were drawn from a distribution of fitness effects, and thus all had different selection coefficients, this would be more complicated.

The recipes in section 9.4.1, on the other hand, can in fact be improved by rewriting them to use `setSelectionCoeff()`. Here is a modified version of the first recipe from that section, which used a `fitness()` callback to model a dominant frequency-dependent mutation type:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);    // neutral
    initializeMutationType("m2", 1.0, "f", 0.1);    // balanced
    initializeGenomicElementType("g1", c(m1,m2), c(999,1));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
```

```
1 { sim.addSubpop("p1", 500); }
late() {
    m2muts = sim.mutationsOfType(m2);
    freqs = sim.mutationFrequencies(NULL, m2muts);
    for (index in seqAlong(m2muts))
       m2muts[index].setSelectionCoeff(0.5 - freqs[index]);
}
10000 { sim.simulationFinished(); }
```

Note that this recipe uses a dominance coefficient of `1.0`, to match the behavior caused by the `fitness()` callback in the section 9.4.1's first recipe; any dominance coefficient could be used here, however. The `late()` event here calculates the frequency of each `m2` mutation, and then uses a loop to set the selection coefficient of each mutation accordingly. The recipe in section 9.4.1 used a fitness formula of `1.5-frequency` in its callback, but here we use `0.5-frequency`; this is because `fitness()` callbacks return relative fitness values, where `1.0` is neutral, whereas with selection coefficients – the currency in which the present recipe trades – `0.0` is neutral instead. As always, this distinction should be treated with care since it is a common cause of errors.

This recipe runs about two orders of magnitude faster than the original recipe – not a small difference. It might not produce exactly identical results, because of the aggregated effects of tiny differences in floating-point roundoff error due to the different way in which fitness values are juggled in the two models, but it is effectively identical for all practical purposes.

However, this recipe's strategy using `setSelectionCoeff()` only works because this is a single-subpopulation model; with multiple subpopulations, one would presumably want the frequency-dependent effect to be different in each subpopulation, and to depend upon the frequency within that subpopulation. Such a model could no longer be achieved using `setSelectionCoeff()`. Section 9.4.1 thus presented a more generally applicable recipe, albeit a slower one.

10. Selective sweeps

This chapter shows how SLiM can be used to model selective sweeps and various associated phenomena such as hitchhiking, background selection, and genetic draft. SLiM's ability to accurately model such scenarios is the origin of its name, **S**election on **Li**nked **M**utations. This chapter will use very simple one-population models; of course these recipes can be combined with the recipes of previous chapters to model sweeps with complex demography and population structure, complex genetic architecture, spatiotemporal variation in selection, and so forth.

10.1 Introducing adaptive mutations

The simplest selective sweep scenario is of an explicitly introduced adaptive mutation sweeping against a background of neutral mutations. We can simulate such a sweep in just a few lines:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 1.0, "f", 0.5);  // introduced mutation
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
1000 late() {
    target = sample(p1.genomes, 1);
    target.addNewDrawnMutation(m2, 10000);
}
10000 { sim.simulationFinished(); }
```

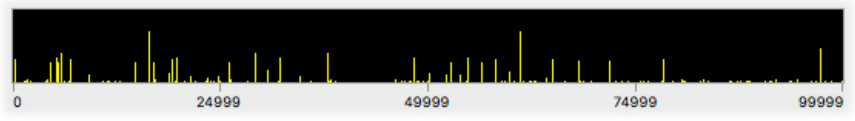
The call to `initializeMutationType()` sets up `m2`, a new mutation type used to represent the introduced beneficial mutation. Note that a dominance coefficient of `1.0` (fully dominant) is used with a selection coefficient of `0.5`; these values provide strong selection for the introduced mutation, making it less likely to be lost due to genetic drift while still at low frequency. This is useful for illustrative purposes here, but of course in real simulations less favorable values would likely be needed, making it more probable that the mutation would be lost rather than sweeping. There are two ways to handle this. One is to simply accept that some runs of the simulation will fail to sweep – do many runs of the model, and collect statistics only across those runs where the sweep succeeds. The second way to handle the problem is to write additional Eidos code to make the simulation run conditional on fixation (see the next section).

The other interesting code here is the Eidos event at generation `1000`. The first line of this event selects a target genome into which the added mutation will be placed. It does this using the `sample()` function, by drawing a single sample from subpopulation `p1`'s vector of genomes. This is important, because SLiM does *not* – for reasons of speed – guarantee a random order to the individuals in a subpopulation. In this simple model all individuals are produced identically, so this is not an issue, but if features of SLiM are used such as migration, separate sexes, selfing, cloning, or `mateChoice()`/`modifyChild()`/`recombination()` callbacks, the individuals in the subpopulation will be produced in a specific and non-random order, and thus whenever a random individual is desired `sample()` must be used (rather than just using the genome at index `0` in the subpopulation, for example).

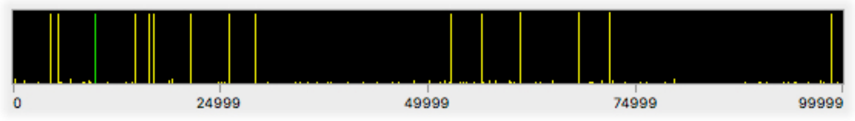
The second line then adds a new mutation to the target genome, drawn from mutation type `m2`; the remaining parameter specifies the position of the mutation in the chromosome as `10000` (this could be drawn randomly using `sample()` as well, if desired).

Note that this event is a late() event, specified in its declaration. These were introduced back in section 4.2.1 as a way to make scripted events happen late in the generation, after offspring generation has occurred (see the generation life cycle overview in section 1.3). It is important that introducing new mutations occurs in a late() event, because it makes script-introduced mutations act in exactly the same way as mutations added by SLiM due to the normal process of mutation during offspring generation. If this event were an early() event instead (as is the default if no explicit designation is given), the mutation would be introduced immediately before offspring generation, and it would have no effect on fitness values since fitnesses would have been calculated before it was added (at the end of the preceding generation). The mutation would therefore be subject to one generation of drift before its correct fitness effect would be accounted for. This would likely not be the desired behavior, so SLiM will issue a warning if you add a mutation during an early() event – you can delete the late() designation here to see that.

The introduced mutation in this model typically sweeps quite quickly (or is lost almost immediately due to drift), so perhaps the simplest way to see what is going on in SLiMgui is to recycle and then enter 1000 in the generation textfield and press return (as illustrated in section 5.1.2). The simulation will advance to the beginning of generation 1000, and you can then press Step to single-step forward and watch the progress of the introduced mutation. Alternatively, you could slow down the simulation speed using the speed slider (as illustrated in section 5.2.2) to see the simulation play more slowly. In either case, you should observe that at generation 1000, just before the beneficial mutation is introduced, there is lots of neutral diversity across the chromosome:



But just before the mutation finishes sweeping (assuming it is not lost – you may need to recycle and repeat this procedure several times to get a run in which the sweep establishes), most of that diversity has been lost, and just a few neutral sites have hitchhiked along with the introduced mutation, producing the characteristic signature of a selective sweep (Smith & Haigh 1974):



Note the green line at position 10000, representing the beneficial mutation itself.

We can automatically halt the model immediately after the introduced mutation has fixed (or has been lost). This requires just a simple modification of the final line of the model, with the call to simulationFinished():

```
1000:10000 late() {
    if (sim.countOfMutationsOfType(m2) == 0)
      sim.simulationFinished();
}
```

Now simulationFinished() is called immediately when the number of mutations of mutation type m2 falls to zero, which happens either when the introduced mutation fixes (because SLiM then converts the mutation into a substitution object), or when it is lost. Note the generation range of 1000:10000 on this event; this means that this termination condition will be checked each generation from 1000 (when the introduced mutation originates) until 10000 (when the model ends, regardless). Also note that a `late()` designation has been added, so that the simulation ends in the same generation that the `m2` mutation is lost or fixed.

It might be nice to have some indication, in the output stream of the simulation, as to whether the introduced mutation fixed or was lost. One simple way to do this is to check for a `Substitution` object of the right mutation type, in a small extension to the event above:

```
1000:100000 late() {
    if (sim.countOfMutationsOfType(m2) == 0)
    {
       fixed = (sum(sim.substitutions.mutationType == m2) == 1);
       cat(ifelse(fixed, "FIXED\n", "LOST\n"));
       sim.simulationFinished();
    }
}
```

The variable `fixed` is assigned a `logical` value that comes from checking the list of substitutions for elements with mutation type `m2`. Each match will produce a value of `T` in the `logical` vector that results from the == operator; and since `T` is equal to `1` in Eidos, whereas `F` is equal to `0`, the `sum()` function then adds up the total number of matches. If the sum is `1`, the mutation fixed; otherwise (when it is `0`) the mutation was lost.

The next line calls `cat()` to concatenate a `string` to the output stream. The `string` comes from the `ifelse()` function, which looks at the `logical` value of its first parameter (`fixed`) and returns its second parameter (`"FIXED\n"`) if that value is `T`; otherwise, it returns its third parameter (`"LOST\n"`). This function is based on the `ifelse()` function of R; it is similar to the "trinary conditional" operator, `?:`, of C and other languages, but `ifelse()` is a vectorized function and can thus perform this operation across whole vectors at once – a useful tool. Even when using it with singletons, as here, it is a compact way to express things that would otherwise require an `if–else` construct and other complications, as in the alternative way of coding this output directive:

```
if (fixed)
    cat("FIXED\n");
else
    cat("LOST\n");
```

10.2 Making sweeps conditional on fixation

The recipe in the previous section did not guarantee that the introduced mutation would sweep to fixation. That is not necessarily a flaw; sometimes one is interested in the outcome of a model both when a sweep completes and when it does not. Sometimes, however, one wishes to make a model that guarantees that a sweep completes:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 1.0, "f", 0.5);  // introduced mutation
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    // save this run's identifier, used to save and restore
    defineConstant("simID", getSeed());

    sim.addSubpop("p1", 500);
}
```

```
1000 late() {
    // save the state of the simulation
    sim.outputFull("/tmp/slim_" + simID + ".txt");

    // introduce the sweep mutation
    target = sample(p1.genomes, 1);
    target.addNewDrawnMutation(m2, 10000);
}
1000:100000 late() {
    if (sim.countOfMutationsOfType(m2) == 0)
    {
       fixed = (sum(sim.substitutions.mutationType == m2) == 1);

       if (fixed)
       {
          cat(simID + ": FIXED\n");
          sim.simulationFinished();
       }
       else
       {
          cat(simID + ": LOST – RESTARTING\n");

          // go back to generation 1000
          sim.readFromPopulationFile("/tmp/slim_" + simID + ".txt");

          // start a newly seeded run
          setSeed(rdunif(1, 0, asInteger(2^32) - 1));

          // re-introduce the sweep mutation
          target = sample(p1.genomes, 1);
          target.addNewDrawnMutation(m2, 10000);
       }
    }
}
```

To make a model that is conditional on fixation, there are some simple "solutions" that don't work. You can't force the introduced mutation to increase in frequency each generation; that would produce abnormal evolutionary trajectories that would distort the model dynamics. Similarly, you can't just reintroduce a new mutation if the previous one is lost; in the process of getting lost, the previous mutation may have affected the genetic background. What you really want is that if the introduced mutation has been lost, the simulation gets reset to precisely the same state as it was in prior to the previous introduction, but with a different random number seed to ensure that events take a different course. If you do this repeatedly until the mutation fixes, you have a proper simulation of a selective sweep conditional upon fixation. SLiM provides a convenient solution for this by allowing the user to save the relevant state of a simulation to disk. Doing this is actually pretty simple; there are just a few key steps that need to be taken to save the state and then restore it when we want to try a different trajectory.

First of all, the generation `1` event now stores the initial random number seed, obtained from `getSeed()`, as a constant named `simID`, using the Eidos function `defineConstant()`. Such constants persist until the simulation terminates or is recycled; unlike variables, defined constants do not disappear at the end of the currently executing event in SLiM, but instead go into the global scope. This value is thus a unique identifier for the model run; if many model runs were being done, each would presumably have a different seed, and thus the initial seed identifies the run.

The event in generation `1000` saves the current population state to a file in the `/tmp` directory, a standard place used in all Un*x systems (including Mac OS X) to store temporary files. The filename used inside the `/tmp` directory is generated using string concatenation with the `+` operator (described in detail in the Eidos manual), based on the value stored earlier in `simID`; the temporary file therefore gets named according to the initial random number seed of the run, with a name like `"slim_92631.txt"`. This event also adds the new mutation that we want to sweep. Note that this event is designated as a `late()` event; this is logical, both because it produces output (by saving the simulation state to disk), and because it adds a mutation to the simulation.

The generation `1000:100000` event checks, each generation, whether the introduced mutation is still present. If it has fixed, it prints a message and terminates the simulation. If it has been lost, it prints a message and reads the saved population state back in (which sets the generation counter back to `1000`). It then changes the random number seed, to start a new evolutionary trajectory (reproducible by starting again at the new seed – see section 17.1 for discussion), and then re-introduces the sweep mutation as before. This event is also a `late()` event; this way if the simulation has to be restored to the saved state, it picks up exactly where it was saved out (it should also be a `late()` event because it adds a new mutation). Finally, note that when we set the generation back to `1000`, the generation `1000` event that did our initial setup does not execute again; the events that will run for a given generation are determined at the beginning of that generation and do not change even if `sim.generation` is changed. If we set `sim.generation` to `999` instead, then the generation `1000` event would execute again, in the next generation.

If you recycle and run this model, sometimes the introduced mutation will fix on the first attempt, but sometimes it will take repeated attempts and you will see output like this:

```
1452090492983: LOST – RESTARTING
1452090492983: LOST – RESTARTING
1452090492983: LOST – RESTARTING
1452090492983: FIXED
```

This demonstrates that the model is working as intended; three introduced mutations were lost before the fourth attempt resulted in fixation. You could change the dominance coefficient and selection coefficient of `m2` to be less favorable, which would result in more restarts but should work fine. You could even make `m2` neutral or deleterious, while still making runs conditional on fixation; we'll see an example of that in section 10.6.2. Since the probability of a new neutral mutation drifting to fixation is small, many restarts will be needed, but no harm is done by that.

One caveat is that `outputFull()` writes out only a specific set of information: the subpopulations that exist, the individuals they contain, and the mutations contained by the genomes of those individuals. When `readFromPopulationFile()` is called, any other state associated with the subpopulation, individuals, genomes, and mutations is wiped away. If the model had set up other properties – setting a cloning rate on a subpopulation, say, or setting up values with `tag` or `setValue()` – that state will be lost, and will need to be set up again.

Given the relative complexity of this recipe, most of the other selective sweep recipes in this chapter will assume that conditionality on fixation is not desired, so that their different topics are not obscured by the conditionality machinery. However, the key elements of this recipe can be combined with any selective sweep strategy – or indeed, can be used to make a simulation that is conditional upon any outcome you wish. In the next section, we will see how to make a simulation conditional upon establishment of a mutation, rather than upon fixation.

10.3 Making sweeps conditional on establishment

In the previous section, we saw how to make a model conditional on fixation of the introduced mutation. Sometimes one may want to relax this condition and require only that the mutation reaches a certain threshold frequency at which selection outweighs drift, rendering subsequent loss unlikely. This threshold frequency is commonly referred to as the establishment frequency, and is a function of the selection coefficient of the mutation. Making our model conditional on establishment, rather than fixation, requires just a simple modification to the previous recipe:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 1.0, "f", 0.5);  // introduced mutation
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    // save this run's identifier, used to save and restore
    defineConstant("simID", getSeed());
    
    sim.addSubpop("p1", 500);
}
1000 late() {
    // save the state of the simulation
    sim.outputFull("/tmp/slim_" + simID + ".txt");
    
    // introduce the sweep mutation
    target = sample(p1.genomes, 1);
    target.addNewDrawnMutation(m2, 10000);
}
1000: late() {
    mut = sim.mutationsOfType(m2);
    
    if (size(mut) == 1)
    {
       if (sim.mutationFrequencies(NULL, mut) > 0.1)
       {
          cat(simID + ": ESTABLISHED\n");
          sim.deregisterScriptBlock(self);
       }
    }
    else
    {
       cat(simID + ": LOST - RESTARTING\n");
       
       // go back to generation 1000
       sim.readFromPopulationFile("/tmp/slim_" + simID + ".txt");
       
       // start a newly seeded run
       setSeed(rdunif(1, 0, asInteger(2^32) - 1));
       
       // re-introduce the sweep mutation
       target = sample(p1.genomes, 1);
       target.addNewDrawnMutation(m2, 10000);
    }
}
10000 {
    sim.simulationFinished();
}
```

Much of the machinery here is carried over from the previous recipe; see section 10.2 for discussion of the way the simulation state is saved and restored. Here, however, the **`1000:`** event checks for the existence of the introduced mutation, using `size()`. If it exists, its frequency is checked against the threshold frequency 0.1 (an arbitrary choice that can be adjusted to whatever threshold frequency you wish). If the mutation's frequency is above that threshold, a message is printed and the script block deregisters itself so that further checks are not done – once the mutation has established, the simulation runs freely to its end, whether the mutation is subsequently fixed or lost. (See section 5.1.2 for discussion of `deregisterScriptBlock()`, as well as sections 10.5.3 and 20.11.2). On the other hand, if the introduced mutation no longer exists, the simulation is reset back to the point of introduction, just as in section 10.2.

When this model is run, you will typically see output like:

```
1459603349880: LOST – RESTARTING
1459603349880: LOST – RESTARTING
1459603349880: LOST – RESTARTING
1459603349880: ESTABLISHED
```

10.4 Partial sweeps

Sometimes it is desirable to make a selective sweep stop or change when the sweep mutation reaches a specific frequency. This recipe will initiate a selective sweep with a beneficial mutation, which will convert into a neutral mutation when it reaches a frequency of `0.5`.

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 1.0, "f", 0.5);  // introduced mutation
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
1000 late() {
    target = sample(p1.genomes, 1);
    target.addNewDrawnMutation(m2, 10000);
}
1000:10000 late() {
    mut = sim.mutationsOfType(m2);
    if (size(mut) == 0)
       sim.simulationFinished();
    else if (mut.selectionCoeff != 0.0)
       if (sim.mutationFrequencies(NULL, mut) >= 0.5)
          mut.setSelectionCoeff(0.0);
}
```

Most of this is similar to previous recipes in this chapter; the difference lies in the `1000:10000` event. This event now uses `mutationsOfType()` to recover the introduced mutation object (which, as usual, can't be stored anywhere persistent). If the mutation is no longer present – if `size(mut)` is zero – the simulation terminates; this is equivalent to the `countOfMutationsOfType(m2)` check done in previous recipes. Otherwise, it uses `mutationFrequences()` to check the frequency of the introduced mutation; if it has cleared the 0.5 threshold, it is converted to neutral with `setSelectionCoeff()`. That last bit of code is protected by a test that the selection coefficient has not already been changed; that check is purely for speed, as `mutationFrequencies()` can be slow.

This recipe could incorporate parts of the previous recipes, in order to determine whether the introduced mutation was lost or had fixed, or in order to make the simulation conditional on the mutation reaching the threshold frequency; the basic idea is easily adapted.

10.5 Soft sweeps from *de novo* mutations

In the previous recipes in this chapter, we've seen "hard" selective sweeps originating from a single new mutation. If, on the other hand, a sweep proceeds from multiple copies of the same mutation, present in different individuals, it is termed a "soft" sweep, because it preserves a more diverse genetic background (Messer & Petrov 2013). Soft sweeps can arise from standing genetic variation (seen in section 10.6), or can occur when multiple copies of the same *de novo* mutation arise during a sweep. This section will model the latter scenario, in three different ways.

10.5.1 A soft sweep from recurrent de novo mutations in a large population

In this recipe, we will model a soft sweep by *de novo* mutations generated by SLiM. In order to get a soft sweep to occur from recurrent *de novo* mutations at the same locus, the population needs to be very large or the mutation rate needs to be very high, so that new copies of the mutation tend to arise before the previous copy has fixed. In this recipe, unlike most recipes in this book, we will not model a background of neutral mutations; instead, this is a model of competing beneficial mutations at a single site. We are, in effect, modeling the sweep of multiple, separate instances of a particular single-nucleotide change, such as the transition of a particular nucleotide from G to A (conceptually – SLiM does not model actual nucleotides). The model terminates when the sweep completes: when every individual genome possesses an instance of the mutation, regardless of where and when this instance arose. With no further ado, the recipe:

```
initialize() {
    initializeMutationRate(1e-5);
    initializeMutationType("m1", 0.45, "f", 0.5);  // sweep mutation
    m1.convertToSubstitution = F;
    m1.mutationStackPolicy = "f";
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 0);
    initializeRecombinationRate(0);
}
1 {
    sim.addSubpop("p1", 100000);
}
1:10000 {
    counts = p1.genomes.countOfMutationsOfType(m1);
    freq = mean(asInteger(counts > 0));

    if (freq == 1.0)
    {
       cat("\nTotal mutations: " + size(sim.mutations) + "\n\n");

       for (mut in sortBy(sim.mutations, "originGeneration"))
       {
          mutFreq = mean(asInteger(p1.genomes.containsMutations(mut)));
          cat("Origin " + mut.originGeneration+ ": " + mutFreq + "\n");
       }

       sim.simulationFinished();
    }
}
```

The chromosome is defined as having a single genomic element that spans from position `0` to position `0`: a single base position. This recipe uses a relatively high mutation rate (`1e-5`) with a large population size (`100000`) so that multiple mutations arise at that single site before the sweep completes. An even larger population size could be used with a lower mutation rate (*N*=`1e6` and *u*=`1e-6`, say, or even *N*=`1e7` and *u*=`1e-7`), but the model would take somewhat longer to complete.

There is one unusual complication in this model: SLiM, by default, allows multiple mutations of a given mutation type to occur at the same site in the same individual ("stacked" mutations, as we will call them). In other words, an individual that has already undergone the G-to-A transition might nevertheless be given another mutation at the same site, representing the same G-to-A transition. While this behavior is desirable in many instances, it is inconvenient in this particular model, and so this recipe tells SLiM to use a different behavior: "stacked" mutations will not be allowed, and new mutations that collide with an existing mutation at the same site will be suppressed. This is achieved by setting the `mutationStackPolicy` property of `m1` to `"f"`, which tells SLiM to prevent stacking by keeping only the *first* (thus `"f"`) mutation of type `m1` at a given site (see section 21.9.1 for details). This simplifies the model's code considerably; without this change in policy, the model would have to carefully take account of the possibility of stacking and compensate for it. Note that if this model contained other mutation types as well, those would still be allowed to coexist, both with each other and with an `m1` mutation at the same site; only stacking of `m1` mutations with other `m1` mutations is prevented (by default; see section 21.9.1).

Second, the dominance coefficient of `0.45` for `m1` is actually a special and important value. SLiM tracks each independent origin of the sweep mutation as a separate `Mutation` object; those mutations are all of type `m1`, but they are distinct mutations as far as SLiM is concerned. If an individual has different versions of the sweep mutation in its two genomes, SLiM will evaluate the fitness of that individual according to the fact that it contains two different mutations, each of which is heterozygous, and each of which therefore uses the mutation type's dominance coefficient. The value `0.45` makes this work out, because the relative fitness for one heterozygous mutation is `1.0+0.45*0.5`, which is `1.225`, and then when the relative fitness values for the two mutations are multiplied together, `1.225*1.225=1.5` (almost exactly), and `1.5` is the relative fitness of the sweep mutation when homozygous. In other words, $h=(\mathrm{sqrt}(1+s)-1)/s$, and therefore $(1+hs)^2=1+s$. This model could be written to use a dominance coefficient that did not satisfy this relationship, but a `fitness()` callback would then be needed to produce the desired fitness values.

The `1:10000` event tallies up the overall frequency of the sweep mutation, regardless of which particular `Mutation` objects are possessed by each individual. To do this, it first uses the `countOfMutationsOfType()` method to produce a vector of the number of mutations in each genome in the population. Then it tests `counts > 0`, producing a `logical` vector that is `T` if a genome contains at least one mutation, `F` otherwise. The `asInteger()` function converts that vector to `integer` (where `T` is `1` and `F` is `0`, as defined by Eidos), and `mean()` then computes the frequency of the sweep as the average of those values. If the frequency is equal to `1.0`, the sweep has completed and the simulation is stopped.

This model executes and stops, but it is hard to tell what's going on; there is only a single base position on the chromosome, so all of the mutations are displayed in a single column in SLiMgui's chromosome view. We can sort of see the sweep progressing, but we can't tell how many mutations are involved, or what the distribution of their frequencies might be. The model therefore has some custom output code that processes the final state of the simulation and prints a summary. Because stacking is prevented by `mutationStackPolicy`, as described above, this output code is quite simple; it just loops through all of the mutations in the simulation (sorted by origin generation, using `sortBy()`), and calculates the frequency of each mutation as the average of the values returned by `p1.genomes.containsMutations()` for that mutation – a very similar strategy to the calculation of the overall frequency of the sweep, as described above. Typical output might indicate that 25 mutations existed in the population at the end of the run (and thus participated in the soft sweep), and would then list the final frequencies of those mutations, sorted in ascending order by origin generation:

```
Total mutations: 25

Origin 4: 0.22628
Origin 6: 0.04301
Origin 7: 0.18139
Origin 7: 0.215995
Origin 10: 0.10995
Origin 12: 0.0709
...
```

10.5.2 A soft sweep with a fixed mutation schedule

The previous recipe relied upon SLiM's standard mutation-generation machinery to generate new instances of a mutation that executed a soft sweep. Sometimes one might wish to have more control over the process than that; our next recipe therefore adds the multiple copies of the sweep mutation at predetermined times during the run, according to a scripted schedule:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 1.0, "f", 0.5);// sweep mutation
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
    p1.tag = 0;  // indicate that a mutation has not yet been seen
}
1000:1100 late() {
    if (sim.generation % 10 == 0) {
       target = sample(p1.genomes, 1);
       if (target.countOfMutationsOfType(m2) == 0)
          target.addNewDrawnMutation(m2, 10000);
    }
}
1:10000 late() {
    if (p1.tag != sim.countOfMutationsOfType(m2)) {
       if (any(sim.substitutions.mutationType == m2)) {
          cat("Hard sweep ended in generation " + sim.generation + "\n");
          sim.simulationFinished();
       } else {
          p1.tag = sim.countOfMutationsOfType(m2);
          cat("Gen. " + sim.generation + ": " + p1.tag + " lineage(s)\n");

          if ((p1.tag == 0) & (sim.generation > 1100)) {
             cat("Sweep failed to establish.\n");
             sim.simulationFinished();
          }
       }
    }
    if (all(p1.genomes.countOfMutationsOfType(m2) > 0)) {
       cat("Soft sweep ended in generation " + sim.generation + "\n");
       cat("Frequencies:\n");
       print(sim.mutationFrequencies(p1, sim.mutationsOfType(m2)));
       sim.simulationFinished();
    }
}
```

There's a lot going on here; let's unpack it. First of all, there are a bunch of `cat()` calls to print out diagnostic information about the sweep. A run of this model might produce output like:

```
Gen. 1000: 1 lineage(s)
Gen. 1010: 2 lineage(s)
Gen. 1020: 3 lineage(s)
Gen. 1030: 4 lineage(s)
Gen. 1032: 3 lineage(s)
Gen. 1040: 4 lineage(s)
Gen. 1041: 3 lineage(s)
Sweep ended in generation 1043
Frequencies:
0.55 0.006 0.444
```

Each time a new copy of the sweep mutation is introduced, it produces a new lineage that is conceptually distinct from other lineages containing the same mutation; although each copy of the mutation is identical (same position, same selection coefficient, etc.), SLiM tracks each introduced copy separately, since each is generated with a separate call to `addNewDrawnMutation()`. (If you wanted SLiM to simulate just a single mutation object, without tracking lineages in this way, you could look up the existing mutation object and add it to new individuals with the `addMutation()` method instead.) As the output shows, the number of lineages increases as new copies get added during the soft sweep; sometimes the lineage count goes down, though, as particular lineages go extinct due to genetic drift. The model uses a value stored in `p1.tag` to track the number of lineages; each time that the current lineage count differs from that `tag` value, a new output line is generated. That's the function of the first half of the `1:10000` event: to track the number of lineages, produce output when it changes, and halt the simulation if a hard sweep completes from a single introduced mutation (indicated by the existence of a substitution of type `m2`) or if the sweep fails to establish (indicated by a lack of active sweep mutations, if we're past the end of the mutation introduction period).

The second half of the `1:10000` event detects when the soft sweep has completed, and prints a message giving the generation at which it completed, along with the frequencies of each of the mutational lineages that ended up being part of the completed sweep. These frequencies sum to `1`, indicating that every individual in the population possesses mutations from one or another of those lineages; given that all of the mutational lineages are genetically identical, this means that the mutation has really fixed, even though it is divided into distinct lineages by the design of the simulation. The way this event detects completion might need a bit of explanation. First, `p1.genomes` gives a vector containing the genomes for all individuals in the subpopulation. The method `countOfMutationsOfType(m2)` performs a count on each genome in that vector, and returns a new vector containing the corresponding counts. The `> 0` test then generates a logical vector containing `T` for each genome that had a copy of the sweep mutation; if any genome is still missing the sweep mutation, this vector will have an `F` in that position. Finally, `all()` returns `T` if all of the elements of that logical vector are `T`; if any genome failed the test, `all()` returns F. You can compare this to the strategy for detecting soft sweep fixation used in the previous section, which actually computes the frequency of the sweep.

The `1000:1100` event is the engine that generates the new mutational lineages of the soft sweep. For simplicity, it starts a new lineage every `10` generations, using the modulo operator, `%`, to test for generations which are evenly divisible by `10`; it would of course be trivial to modify this to generate the new lineages at whatever fixed generations you wished, or to generate a new lineage randomly with a given probability. In any case, when it is decided that a new lineage should be created this event adds a new mutation, identical to the previous mutations, to a randomly chosen genome, much as we have seen before.

The only tricky bit here is that we want to prevent more than one sweep mutation from existing in the same individual, so before we add the new mutation, we check whether one is already there. Normally SLiM allows two mutations to occupy exactly the same position in the chromosome; the check here avoids that possibility, so as to guarantee that the final lineage frequencies will sum to exactly `1`. In the previous section, we used the `mutationStackPolicy` property of `MutationType` to prevent such "stacked" mutations; that solution would work equally well here, since the mutation type's stacking policy applies to introduced mutations as well as to mutations generated by SLiM. A different strategy is employed here simply to show a different approach to the same issue.

10.5.3 A soft sweep with a random mutation schedule

As mentioned above, the previous recipe could be modified to follow a random schedule quite easily; for example, the `(sim.generation % 10 == 0)` test could be changed to `(runif(1) < 0.1)` to provide a new mutational lineage at random times averaging every ten generations. But perhaps your model would like to know the mutation schedule ahead of time, for some reason; you would like to have, at the outset, a list of the generations in which a new lineage will be created. This would allow you to prune out schedules that didn't satisfy some criterion, or run statistics on the schedule in advance, or other such tasks. Here is an alternative recipe, then, that generates a schedule ahead of time and then uses it to generate lineages:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 1.0, "f", 0.5);// sweep mutation
    m2.mutationStackPolicy = "f";
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);

    gens = cumSum(rpois(10, 10));      // make a vector of start gens
    gens = gens + (1000 - min(gens));  // align to start at 1000

    for (gen in gens)
       sim.registerLateEvent(NULL, s1.source, gen, gen);

    sim.deregisterScriptBlock(s1);
}
s1 1000 late() {
    sample(p1.genomes, 1).addNewDrawnMutation(m2, 10000);
}
1:10000 late() {
    if (all(p1.genomes.countOfMutationsOfType(m2) > 0))
    {
       cat("Frequencies at completion:\n");
       print(sim.mutationFrequencies(p1, sim.mutationsOfType(m2)));
       sim.simulationFinished();
    }
    if ((sim.countOfMutationsOfType(m2) == 0) & (sim.generation > 1100))
    {
       cat("Soft sweep failed to establish.\n");
       sim.simulationFinished();
    }
}
```

The `1:10000` event checks for loss or completion of the sweep and reacts accordingly, much as we have seen previously. This recipe has been simplified somewhat from the previous one, for brevity, however; some of the output has been removed, the lineage-counting mechanism using `p1.tag` has been removed, and if the final result is a hard sweep this recipe considers it as a "failure to establish", unlike the previous recipe – after all, the goal is to produce a soft sweep. Of course those pieces could be added back in to this recipe if desired. "Stacked" mutations are prevented here using `mutationStackPolicy`, as in section 10.5.1 but unlike section 10.5.2, to show the alternative approach in a model using introduced mutations (see those sections for further discussion of the issue of stacked mutations).

More interesting is how the lineage addition works now. There is an event declared using a syntax that has not been seen up until now:

```
s1 1000 late() {
```

This event is *named*; an Eidos constant, `s1`, will be defined as referring to the script block for the event. To some extent this is just a shorthand for convenience; all defined script blocks in a simulation are available through `sim.scriptBlocks`, as objects of type `SLiMEidosBlock`, and this block could be looked up from that vector using the properties of that class (by looking for a block running only in generation `1000`, for example). Being able to just use the name `s1` is obviously more convenient, and mirrors the syntax of being able to refer to a subpopulation as `p1`, a genomic element type as `g1`, or a mutation type as `m1`.

Putting that aside, this event schedules the addition of a new lineage in much the same way as in the previous recipe. Notably, however, the generation `1000` event now schedules a new lineage just once. The trick behind this recipe is that this block gets re-scheduled by the model to run in an assortment of other generations. The code to do this is in the generation `1` event. First, a vector of all the generations in which the event will run is constructed by drawing from a Poisson distribution to get waiting times, using `rpois()`, and then calculating cumulative sums from that vector of waiting times, using `cumSum()`; the Eidos documentation gives details on these functions, of course. This vector is then realigned so that its smallest element is equal to `1000`, giving us the final schedule of lineage additions that will be followed. The event then loops through that vector, and for each generation in it, it calls `sim.registerLateEvent()` to schedule a lineage addition in that generation. It does this by scheduling the source code from the `s1` event over again, obtained simply with `s1.source`. Finally, the `s1` event itself is deregistered; the loop has already scheduled a lineage addition in generation `1000`, so `s1` is not needed. In this way, `s1` itself never runs at all, but its source code is used as a template for ten other events that do run.

The fact that Eidos is an interpreted language gives you the freedom to play all sorts of games like this with the code of your simulation, even as it runs; you can register new events and callbacks, deregister existing ones, and even generate code on the fly and then execute it with the `executeLambda()` command. These sorts of techniques should be used in moderation, as they can make the code of a model difficult to understand and maintain; but in some situations, as here, they can prove exceedingly useful for implementing highly dynamic model behavior.

Incidentally, SLiMgui provides graphical tools for inspecting the event list, which can be useful for understanding the behavior of models like this. This feature was previously described in section 5.1.2, in a very different context; you might try opening the window drawer as described in that section, and then recycling this model and stepping through generation `1`. You will see that initially, the event list contains `s1`; after generation `1` has executed, `s1` has disappeared from the list, because it has been deregistered, and ten new events have been added programmatically.

10.6 Sweeps from standing genetic variation

The previous section showed recipes for simulating soft selective sweeps with *de novo* mutations – either introduced explicitly, or resulting from the normal mutational processes of SLiM. Soft sweeps can also originate from standing genetic variation, however. In this case, a mutation that was previously neutral becomes beneficial (presumably due to a change in the environment), suddenly exposing the mutation to selection. Because the mutation was initially neutral, it will generally occur in the population against a variety of genetic backgrounds; a soft selective sweep will therefore generally occur, although a hard sweep is possible if just one of the mutation-containing lineages happens to eliminate all of the others.

There are several ways that a sweep from standing genetic variation might be modeled. We will examine two recipes in this section: a sweep from standing variation at a randomly chosen locus, and a sweep from standing variation at a predetermined locus that is triggered when a mutation at that locus reaches a threshold frequency.

10.6.1 A sweep from standing variation at a random locus

In this first recipe, a randomly chosen mutation will be picked out of the standing neutral genetic diversity that has accumulated in the model; the only criterion for the selection of the mutation will be that it must be above a threshold frequency. The chosen mutation will be changed to be beneficial (reflecting an environmental change), and the model will terminate when the mutation has either been lost or has completed a sweep:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 1.0, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
}
1000 late() {
    muts = sim.mutations;
    muts = muts[sim.mutationFrequencies(p1, muts) > 0.1];

    if (size(muts))
    {
       mut = sample(muts, 1);
       mut.setSelectionCoeff(0.5);
    }
    else
    {
       cat("No contender of sufficient frequency found.\n");
    }
}
1000:10000 late() {
    if (sum(sim.mutations.selectionCoeff) == 0.0)
    {
       if (sum(sim.substitutions.selectionCoeff) == 0.0)
          cat("Sweep mutation lost in gen. " + sim.generation + "\n");
       else
          cat("Sweep mutation reached fixation.\n");
       sim.simulationFinished();
    }
}
```

The generation `1000` event chooses the target mutation and transmogrifies it. The `muts` variable is set up initially as the full set of mutations in the simulation, and is then whittled down to only those mutations above a minimum threshold frequency of `0.1`. Note that it would be straightforward to modify this further and also require that the mutation is below a given maximum threshold frequency; in that case, we would be studying a scenario of a selective sweep from a standing genetic variant with starting frequency within the interval (min, max). The `sample()` function is then used to choose one mutation from that set, at random, and the chosen mutation has its selection coefficient altered to be beneficial. Note that this event is a `late()` event; this is for essentially the same reasons as explicated in section 4.2.1. We are changing the selection coefficient of an existing mutation; for the fitness effect of that change to be realized immediately, it must happen in a `late()` event so that the change occurs after offspring generation but before fitness recalculation.

The `1000:10000` event just checks for termination conditions: either the chosen mutation has been lost, or it has fixed. Since a separate mutation type is not used for the sweep mutation in this model, unlike the other sweep models we have seen, these termination conditions are detected using the property that the chosen mutation has a non-zero selection coefficient.

This could be tailored in all sorts of ways; for example, the transition from neutral to beneficial could be made gradual, or the new selection coefficient could be drawn from a distribution rather than being a fixed value.

10.6.2 A sweep from standing variation at a predetermined locus

In this recipe we want to model a soft sweep from standing genetic variation. Specifically, we want to assume that a previously neutral mutation suddenly becomes beneficial as a consequence of an environmental change, and then subsequently sweeps in the population. In this scenario, we can choose the "starting frequency" of the mutation at the time the environment changes. Our recipe for this scenario is based on the conditional-on-establishment machinery of section 10.3, which restarts the simulation if the mutation is lost prior to reaching the chosen starting frequency (here defined as a frequency of `0.1`). If the mutation does manage to drift to this frequency, it is then converted to be beneficial. After that point, the model runs without conditionality, and detects whether the mutation fixes or is lost prior to generation `10000`.

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 1.0, "f", 0.0);  // introduced mutation
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    // save this run's identifier, used to save and restore
    defineConstant("simID", getSeed());

    sim.addSubpop("p1", 500);
}
1000 late() {
    // save the state of the simulation
    sim.outputFull("/tmp/slim_" + simID + ".txt");

    // introduce the sweep mutation
    target = sample(p1.genomes, 1);
    target.addNewDrawnMutation(m2, 10000);
}
```

```
1000: late() {
    mut = sim.mutationsOfType(m2);

    if (size(mut) == 1)
    {
       if (sim.mutationFrequencies(NULL, mut) > 0.1)
       {
          cat(simID + ": ESTABLISHED – CONVERTING TO BENEFICIAL\n");
          mut.setSelectionCoeff(0.5);
          sim.deregisterScriptBlock(self);
       }
    }
    else
    {
       cat(simID + ": LOST BEFORE ESTABLISHMENT – RESTARTING\n");

       // go back to generation 1000
       sim.readFromPopulationFile("/tmp/slim_" + simID + ".txt");

       // start a newly seeded run
       setSeed(rdunif(1, 0, asInteger(2^32) - 1));

       // re-introduce the sweep mutation
       target = sample(p1.genomes, 1);
       target.addNewDrawnMutation(m2, 10000);
    }
}
1000:10000 late() {
    if (sim.countOfMutationsOfType(m2) == 0)
    {
       fixed = (sum(sim.substitutions.mutationType == m2) == 1);
       cat(simID + ifelse(fixed, ": FIXED\n", ": LOST\n"));
       sim.simulationFinished();
    }
}
```

Most of the code here is identical to the recipe in section 10.3, so please refer to that section for further discussion. Compared to that recipe, mutation type `m2` now has an initial selection coefficient of `0.0`, making it neutral. If the mutation reaches the threshold frequency of `0.1`, an extra line of code calls `setSelectionCoeff()` to convert the mutation to beneficial. Finally, a `1000:10000` event has been added that checks for fixation or loss. Note that this event runs after the `1000:` event, because it is declared later in the source code; the `1000:` event catches cases of loss prior to establishment and restarts the model before the `1000:10000` event notices the loss.

If you run this model, it will probably emit a long string of restart messages before it fixes, due to loss of the introduced mutation while it is still neutral. Once it reaches the threshold frequency and is converted to beneficial, it will usually fix. Typical output is therefore something like:

```
1460585630465: LOST BEFORE ESTABLISHMENT – RESTARTING
1460585630465: LOST BEFORE ESTABLISHMENT – RESTARTING
...
1460585630465: LOST BEFORE ESTABLISHMENT – RESTARTING
1460585630465: LOST BEFORE ESTABLISHMENT – RESTARTING
1460585630465: ESTABLISHED – CONVERTING TO BENEFICIAL
1460585630465: FIXED
```

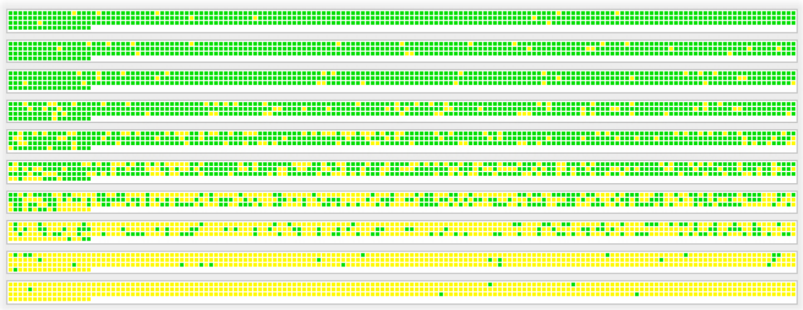
It would be simple to convert the introduced mutation to be initially deleterious; the model would still work. In that case, however, it would usually take a very long time to complete a run, because the introduced mutation would frequently be lost unless we chose a very low threshold frequency.

10.7 Adaptive introgression

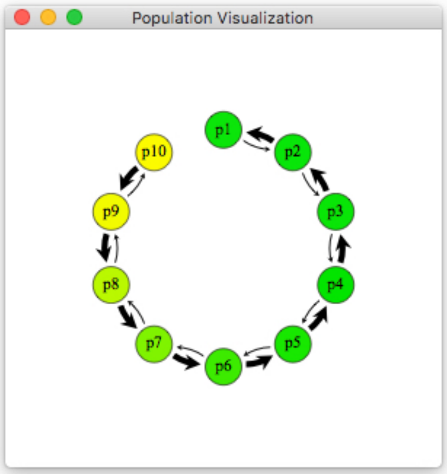
All of the selective sweep recipes thus far have involved just a single subpopulation. Here we want to extend this to model adaptive introgression, the progress of an adaptive allele from its subpopulation of origin into another subpopulation via migration and gene flow. Section 5.3 introduced techniques for setting up structured populations with migration; all we need to do is add a selective sweep to such a model. Here's a simple model combining the population structure of section 5.3.1's recipe with the hard sweep dynamics of section 10.1 (both slightly modified):

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 1.0, "f", 0.5);// introduced mutation
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    subpopCount = 10;
    for (i in 1:subpopCount)
       sim.addSubpop(i, 500);
    for (i in 2:subpopCount)
       sim.subpopulations[i-1].setMigrationRates(i-1, 0.01);
    for (i in 1:(subpopCount-1))
       sim.subpopulations[i-1].setMigrationRates(i+1, 0.2);
}
100 late() {
    target = sample(p1.genomes, 1);
    target.addNewDrawnMutation(m2, 10000);
}
100:100000 late() {
    if (sim.countOfMutationsOfType(m2) == 0)
    {
       fixed = (sum(sim.substitutions.mutationType == m2) == 1);
       cat(ifelse(fixed, "FIXED\n", "LOST\n"));
       sim.simulationFinished();
    }
}
```

If you run this model and stop the run in the middle, while the adaptive introgression is in progress (assuming it is not lost by chance early on – you may have to recycle and restart several times before it catches), the population shown in SLiMgui may look something like this:



Individuals possessing the introgressing allele are colored green; note that there are no intermediate-colored individuals because `m2` is fully dominant. The mutation was introduced into subpopulation `p1`, and so it is closest to fixation there, whereas it has only just begun to sweep in `p10`. Of course it is not possible to see the connectivity between the subpopulations, and the migration rates between them, in this view. As described in section 5.1.3, you can open the population visualization window to see what the population structure looks like:



Here we see that we have a stepping-stone model, with gene flow mostly from `p10` toward `p1`, opposing the spread of the introduced mutation. Nevertheless, the mutation introgresses quite rapidly given the parameters for this model; you could play with migration rates, selection coefficients, etc. to test how they affect the time until completion of the sweep. It would be easy to introduce spatial variation in selection into this model, too, using the techniques of section 9.2, in order to allow the introgression to proceed only so far along the chain of subpopulations before further introgression is blocked by local selection against it (see section 12.3).

10.8 Fixation probabilities under Hill-Robertson interference

In this final section, we'll see how a simple sweep model can test the predictions of population genetic theory. The recipe here will model Hill-Robertson interference, the interference of beneficial mutations that have arisen in different lineages and thus compete against each other (Hill & Robertson 1966). The recipe's code then compares the predicted mean fixation time for a beneficial allele without such interference to the actual mean fixation time observed by the simulation.

The design of this recipe is that the first `5000` generations of the run are a burn-in period during which a dynamic equilibrium is reached, and then the final `1000` generations are measured. The formulas for the probability of fixation of a beneficial mutation without interference and the expected number of fixed mutations are calculated according to standard population genetic theory (Kimura 1962). The actual number of fixed mutations is obtained from the information stored in SLiM's substitution objects, which record the generation of fixation of all mutations; the number of fixed mutations with a generation of fixation after the end of the burn-in can then be counted. As we shall see below, the actual count is much lower than the expected count; fixation is being highly suppressed in this model compared to the expectations without Hill-Robertson interference.

Without further ado, the recipe:

```
initialize() {
    initializeMutationRate(1e-6);
    initializeMutationType("m1", 0.5, "f", 0.05);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 1000);
}
6000 late() {
    // Calculate the fixation probability for a beneficial mutation
    s = 0.05;
    N = 1000;
    p_fix = (1 - exp(-2 * s)) / (1 - exp(-4 * N * s));

    // Calculate the expected number of fixed mutations
    n_gens = 1000;  // first 5000 generations were burn-in
    mu = 1e-6;
    locus_size = 100000;
    expected = mu * locus_size * n_gens * 2 * N * p_fix;

    // Figure out the actual number of fixations after burn-in
    subs = sim.substitutions;
    actual = sum(subs.fixationGeneration >= 5000);

    // Print a summary of our findings
    cat("P(fix) = " + p_fix + "\n");
    cat("Expected fixations: " + expected + "\n");
    cat("Actual fixations: " + actual + "\n");
    cat("Ratio, actual/expected: " + (actual/expected) + "\n");
}
```

Running this produces output like this (a typical result):

```
P(fix) = 0.0951626
Expected fixations: 19032.5
Actual fixations: 302
Ratio, actual/expected: 0.0158676
```

This is obviously a very simple model; the point is just to demonstrate that it is straightforward to make models that test theoretical predictions like this – and that Hill-Robertson interference can make a large difference to dynamics! If you run the model in SLiMgui, the way that the competition of different lineages slows progress towards fixation is quite apparent. Of course if the mutational input is constant, and the time to fixation increases, that has to mean (assuming equilibrium) that fewer mutations are fixing. That can also be observed with this model in SLiMgui; you can see many substantial bars, representing beneficial mutations at reasonably high frequencies, getting pushed down to zero by the rise of a competing haplotype. Far fewer beneficial mutations would be lost if they were not competing with each other. Recombination occasionally resolves these conflicts by bringing competing mutations together onto the same chromosome.

A very simple way to check this model is to decrease the mutation rate. The lower the mutation rate, the less competition there should be between different mutations existing simultaneously in the population (to the limiting case of a single extant mutation at any given time, which would experience no Hill-Robertson interference at all). This is very easy to test; just change the mutation rate to `1e-7`, both where it is set with `initializeMutationRate()` and where it is assigned to the variable `mu` for the calculations at the end. With both of those set to `1e-7`, typical output is something like:

```
P(fix) = 0.0951626
Expected fixations: 1903.25
Actual fixations: 88
Ratio, actual/expected: 0.0462367
```

And if we change the rate to `1e-8`, again in both places, we get:

```
P(fix) = 0.0951626
Expected fixations: 190.325
Actual fixations: 16
Ratio, actual/expected: 0.0840667
```

With `1e-9`, we get something like this (with a lot of stochasticity in the result, at this point – `1000` generations post-burn-in is not nearly long enough to get an accurate estimate of the model's behavior when the mutation rate is so low):

```
P(fix) = 0.0951626
Expected fixations: 19.0325
Actual fixations: 6
Ratio, actual/expected: 0.31525
```

So as predicted, the lower the mutation rate, the less Hill-Robertson interference influences the dynamics, and the more closely the model approximates the theoretical ideal of independent mutations without interference. And indeed, if you run the model with the mutation rate of `1e-9` in SLiMgui, you will see that sometimes multiple mutations still interfere, but fairly often, too, single mutations arise and fix individually. Of course a rigorous analysis would want to use a longer burn-in, a longer post-burn-in runtime, multiple runs averaged together for each mutation rate, calculation of a standard error of the mean across each set of multiple runs, statistical tests for significance of differences, and so forth; but even this very simple analysis is sufficient to make the trend quite clear.

11. Complex mating schemes

Since SLiM is based on the Wright-Fisher model, biparental mating in SLiM is normally random; for each offspring individual to be generated in a subpopulation, two parents are chosen at random from the appropriate subpopulation (which may not be the same subpopulation as the offspring's subpopulation, if migration is involved). It is possible to modify this default behavior, however, by writing a special type of Eidos script block called a `mateChoice()` callback. These callbacks are documented comprehensively in the SLiM reference, in section 22.3. Here we will explore recipes that illustrate the use of `mateChoice()` callbacks to implement two different types of non-random mating: assortative mating, and sequential mate search.

Some mating schemes are actually better modeled using a different type of callback, a `modifyChild()` callback. Mostly, `modifyChild()` callbacks are used for purposes other than mating schemes; recipes using them are mostly in chapter 12 (and they are documented in the SLiM reference in section 22.4). However, the last recipe in this chapter will implement an interesting type of non-random mating, gametophytic self-incompatibility based on an S-locus, using a `modifyChild()` callback. See section 13.7 for another type of non-random mating, forcing SLiM to execute a specified pedigree, also done with a `modifyChild()` callback.

11.1 Assortative mating

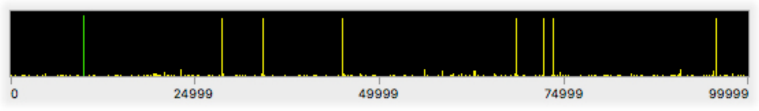
Assortative mating is the preference of an individual for mates that resemble the individual itself in some way. A species could exhibit assortative mating by size, for example, which would mean that smaller individuals tend to prefer other smaller individuals as mates, whereas larger individuals tend to prefer other larger individuals. Assortative mating is an important topic in evolutionary biology because it is thought to be important to the process of speciation: a population can diverge into genetically distinct lineages if assortative mating becomes strong enough to reproductively isolate phenotypically distinct subsets of the population from each other. Indeed, this mechanism can be so effective that if a single gene provides both adaptive phenotypic divergence and assortative mating based upon the diverging trait, the trait governed by the gene is called a "magic trait" because of its power to facilitate speciation (Servedio et al. 2011).

In this section we'll look at a simple magic-trait model in SLiM (see sections 13.1 and 14.8 for further investigations of this topic). Since this is a relatively complex model, let's put it together one piece at a time. The first piece is to set up the genetic and population structure:

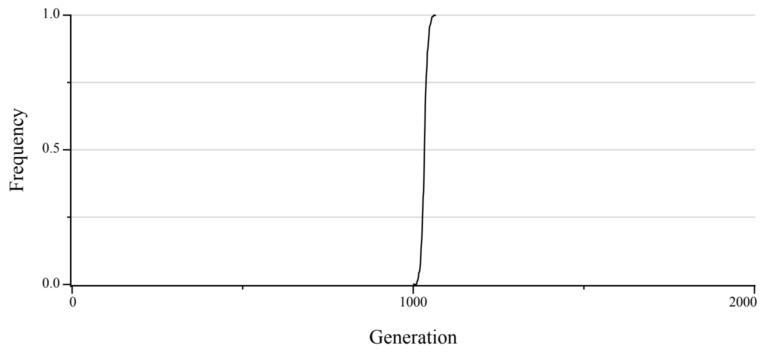
```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 1.0, "f", 0.5);  // introduced mutation
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
    sim.addSubpop("p2", 500);
    p1.setMigrationRates(p2, 0.1);
    p2.setMigrationRates(p1, 0.1);
}
1000 late() {
    target = sample(p1.genomes, 1);
    target.addNewDrawnMutation(m2, 10000);
}
3499 { sim.simulationFinished(); }
```

This is very similar to the "introduced adaptive mutation" recipe of section 10.1: we have two mutation types, one neutral (`m1`) and the other adaptive (`m2`), and after running a burn-in period of `1000` generations using only type `m1`, we introduce a single mutation of type `m2` into a randomly chosen genome. The main difference between section 10.1's recipe and this model is that here we have two subpopulations connected by migration; the gene flow introduced by the migration rate of `0.1` in both directions between the subpopulations is substantial.

When run, this model provides sweep dynamics similar to those seen in some recipes in the previous chapter. In the snapshot below, most of the neutral diversity has been swept away by the beneficial mutation introduced at position `10000`, which is about to fix and is carrying a few neutral mutations along with it:



We can also examine the behavior of this model in SLiMgui using the Mutation Frequency Trajectories graph. First recycle the simulation, then click the Show Graph popup button and open the Mutation Frequency Trajectories graph window from that menu. At this point, the simulation is not yet initialized, and so the graph is empty. Step forward one generation, over the `initialize()` callback; now the mutation types have been defined, and so you can choose mutation type `m2` from the popup in the graph window. Play the simulation forward, and you should end up with a plot something like this, if the introduced mutation is not lost (if it is lost, you can just recycle and try again):



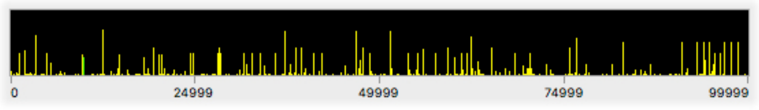
This plot illustrates that from the point at which the mutation was introduced, in generation 1000, it swept very rapidly to fixation.

For our magic-trait model we need divergent ecological selection between the subpopulations, which we introduce by adding a `fitness()` callback that flips the fitness effect of the introduced mutation in subpopulation `p2`:

```
fitness(m2, p2) { return -0.2; }
```

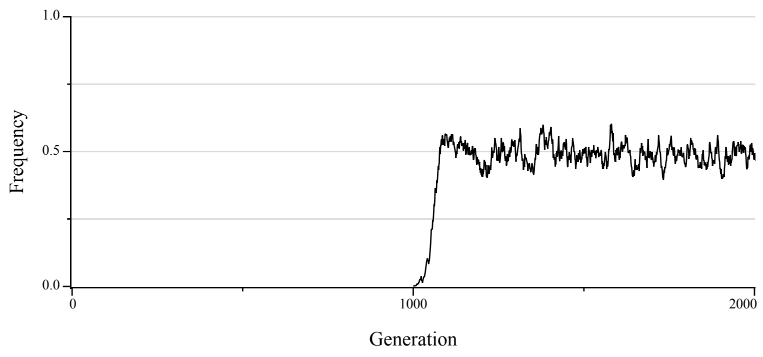
That's all it takes. For simplicity, we are modeling a dominant mutation here, but we could easily use a scheme such as that in section 9.4.1 if the mutation were not dominant.

A little while after the introduced mutation arose, this looks like:



The introduced mutation is not fixing in this version of the model; indeed, it is stuck fluctuating around a frequency of 0.5, unable to increase further because it is deleterious in `p2`. Note that there is lots of neutral variation in this run, in contrast to the previous version of the model.

If we look at the Mutation Frequency Trajectories graph now, we see a very different pattern, illustrating how the spatial variation in selection is preventing the introduced mutation from fixing:



Finally, for a magic-trait model we need assortative mating based upon the same locus that is under divergent selection. In this model, that assortative mating will be provided by a `mateChoice()` callback, which we can add now:

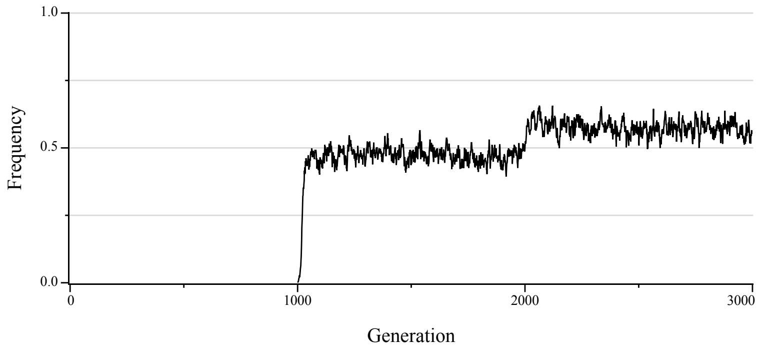
```
2000: mateChoice() {
    parent1HasMut = (individual.countOfMutationsOfType(m2) > 0);
    parent2HasMut = (sourceSubpop.individuals.countOfMutationsOfType(m2)
       > 0);
    if (parent1HasMut)
       return weights * ifelse(parent2HasMut, 2.0, 1.0);
    else
       return weights * ifelse(parent2HasMut, 0.5, 1.0);
}
```

This callback is a bit complicated, so let's walk through it. The first line determines whether the parent that is choosing a mate possesses the magic-trait mutation. The choosing parent is provided to the callback as an object named `individual`, of class `Individual`; this class is essentially a bag containing the two `Genome` objects belonging to the individual. The `countOfMutationsOfType()` method of `Individual` counts all occurrences of mutations of the given type in both of the individual's genomes; in other words, if the individual is homozygous for a given `m2` mutation, that mutation is represented twice in the count. Comparing the total count to `0` yields a single `logical` truth value indicating whether any mutation of that type is present in the individual. Note that the use of `> 0` means that we are ignoring dominance; for purposes of mate choice, we are treating the mutation as dominant. If we wanted heterozygotes to prefer heterozygotes and homozygotes prefer homozygotes, or some such mating scheme, we could use the actual count instead; with a little change to the following logic that would work fine too.

Similarly, we can assess whether the other individuals in the subpopulation – the potential mates – possess the mutation using `countOfMutationsOfType(m2)` for all the individuals in the subpopulation. As previously, we use a `> 0` comparison to get a vector of `logical` values, `parent2HasMut`, indicating whether each individual in the subpopulation possess the magic-trait mutation in either of its genomes.

Finally, we have a little logic at the end to determine the mating preferences we want to return. The standard fitness-based mating weights are supplied to the `mateChoice()` callback in the weights variable, and we don't want to ignore that; if we didn't use that vector at all, we would be overriding SLiM's built-in fitness calculations, based on the selection coefficients of mutations, entirely (which you may do if you wish, but which is usually not what is wanted). Here, we start with `weights`, and combine it multiplicatively with an assortative-mating term computed with `ifelse()`. The `ifelse()` function produces a result by looking at each element of its first parameter (here, `parent2HasMut`) and choosing a corresponding element for the result; if the element from the first parameter is `T`, an element from the second parameter is chosen, whereas if the element from the first parameter is `F`, an element from the third parameter is chosen. The second and third parameters may be non-singleton vectors, too; `ifelse()` is a very powerful vectorized comparison function, which you can read more about in the Eidos documentation. Here, its use is really quite simple. If the parent choosing a mate possesses the magic-trait mutation, then candidate mates that also possess it get a multiplier of 2.0, expressing the preference of carriers for other carriers. If the parent choosing a mate does not possess the magic-trait mutation, then candidate mates that possess it get a multiplier of 0.5, expressing the dislike of non-carriers for carriers.

If we recycle and run, and then look at the Mutation Frequency Trajectories graph, we can see the effects of this callback kick in at generation `2000`, when the callback becomes active:



At generation `2000`, when the `mateChoice()` callback becomes active, the frequency of the magic-trait allele jumps upward. If the two subpopulations were able to reach complete reproductive isolation through this mechanism, we would expect the frequency plotted here to equilibrate at `1.0` (because this graph shows the frequencies in subpopulation `p1` only). In practice, full divergence is not possible, because SLiM is a model of juvenile dispersal, and fitness acts during mating (as opposed to causing mortality earlier in the generation life cycle). Given the migration rates declared in the model, approximately 10% of the individuals in each subpopulation will come from matings in the other population, every generation. Those migrants are also mating assortatively – they might be maladapted in their new home, but they will nevertheless preferentially mate with each other to produce offspring that are also maladapted. Given the very high migration rate, adaptive divergence is helped only a little by the addition of assortative mating (but see below).

The rest of the chromosome, outside the magic-trait locus, is subject only to neutral mutations in this simple model. These neutral mutations can provide a means of monitoring the degree of divergence between the subpopulations in the model; if the subpopulations become fully reproductively isolated from each other, divergence at neutral sites should be observed, whereas without reproductive isolation divergence at neutral sites should be small or absent. This is often measured with a metric called F_{ST}: higher F_{ST} indicates greater genetic divergence among subpopulations. We can add code to start calculating the mean F_{ST} between `p1` and `p2` at generation `3000`:

```
// Calculate the FST between two subpopulations
function (f$)calcFST(o<Subpopulation>$ subpop1, o<Subpopulation>$ subpop2)
{
    p1_p = sim.mutationFrequencies(subpop1);
    p2_p = sim.mutationFrequencies(subpop2);
    mean_p = (p1_p + p2_p) / 2.0;
    H_t = 2.0 * mean_p * (1.0 - mean_p);
    H_s = p1_p * (1.0 - p1_p) + p2_p * (1.0 - p2_p);
    fst = 1.0 - H_s/H_t;
    fst = fst[!isNAN(fst)];  // exclude muts where mean_p is 0.0 or 1.0
    return mean(fst);
}

3000: late() {
    sim.setValue("FST", sim.getValue("FST") + calcFST(p1, p2));
}
3499 late() {
    cat("Mean FST at equilibrium: " + (sim.getValue("FST") / 500));
    sim.simulationFinished();
}
```

This recipe introduces a new feature in Eidos that was introduced in SLiM 2.5: user-defined functions (see the Eidos manual for details on the syntax, etc.). Most of the code above defines a new function, named `calcFST()`, that calculates the F_{ST} between two subpopulations. The rest of the code just calls that function, records the results, and prints out a summary at the end of the run (discussed below). Writing a new function like this is a good way to encapsulate general-purpose code that could be reused in other models. In fact, user-defined functions like this have so much potential to be useful that we have started a Github repository just for sharing them with other users of SLiM: https://github.com/MesserLab/SLiM-Extras. Some of the functions shared there have been written by us; we're hoping that SLiM users will contribute more. You can send us a contribution via a git pull request, or you can just email us your code and we'll put it into the repository for you if you prefer. If you're a regular user of SLiM, it might be a good idea for you to check that repository from time to time, to see what new goodies might have been added!

Besides the quirk of the user-defined function, this code is just an Eidos implementation of Wright's definition of F_{ST}:

$$F_{ST} = 1 - \frac{H_S}{H_T}$$

where H_S is the average heterozygosity in the two subpopulations, and H_T is the total heterozygosity when both subpopulations are combined. Note that all of the calculations here are vectorized; the F_{ST} for each mutation in the simulation is calculated simultaneously in the code above, leveraging the vectorized syntax of Eidos, and only at the end (with `mean(F_ST)`) are those values combined into a mean F_{ST} value across the chromosome.

The mean F_{ST} for the generation is added to a value kept by the simulation using its dictionary-like `getValue()` / `setValue()` mechanism (see section 21.12.2), to keep a running total; that total is then used in generation `3499` to calculate the average F_{ST} over the generations `3000:3499`. The `getValue()` / `setValue()` facility simply provides a way to attach named state to the simulation; it is similar to the `tag` property we have used in various other recipes, but is more flexible (allowing us to keep track of state of type `float` here, for example, whereas `tag` is limited to `integer` values).

We also need to add a line to the generation `1` event, to zero out the running F_{ST} total:

```
sim.setValue("FST", 0.0);
```

If we run the model with the `mateChoice()` callback commented out, we get this output at the end of the run (for a run in which the focal mutation is not lost):

```
Mean FST at equilibrium: 0.0208799
```

Running it with the `mateChoice()` callback active, on the other hand, produces this output at the end of the run:

```
Mean FST at equilibrium: 0.0322724
```

The magic trait therefore appears to have increased the level of divergence between the subpopulations at neutral loci, relative to the divergence for the same trait under natural selection but without the "magic" effect on mate choice, due to a decrease in gene flow. Single runs are of course not sufficient to show this convincingly; in practice, you would want to do many replications of both models, and do some statistics to show that the difference between the outcomes of the two models is significant. You might also wish to run for more than `1000` generations before starting to gather the F_{ST} statistics, to assure that equilibrium had been reached. You might also wish to verify that the magic trait was not lost from the simulation; that happens occasionally, which of course defeats the purpose of the model. Finally, you might look separately at the F_{ST} at different positions along the chromosome, since it might be much higher near the magic trait locus than at more distant locations, due to linkage.

For the record, the complete model with all of the above components is:

```
// Calculate the FST between two subpopulations
function (f$)calcFST(o<Subpopulation>$ subpop1, o<Subpopulation>$ subpop2)
{
    p1_p = sim.mutationFrequencies(subpop1);
    p2_p = sim.mutationFrequencies(subpop2);
    mean_p = (p1_p + p2_p) / 2.0;
    H_t = 2.0 * mean_p * (1.0 - mean_p);
    H_s = p1_p * (1.0 - p1_p) + p2_p * (1.0 - p2_p);
    fst = 1.0 - H_s/H_t;
    fst = fst[!isNAN(fst)];  // exclude muts where mean_p is 0.0 or 1.0
    return mean(fst);
}

initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 1.0, "f", 0.5);  // introduced mutation
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.setValue("FST", 0.0);
    sim.addSubpop("p1", 500);
    sim.addSubpop("p2", 500);
    p1.setMigrationRates(p2, 0.1);
    p2.setMigrationRates(p1, 0.1);
}
1000 late() {
    target = sample(p1.genomes, 1);
    target.addNewDrawnMutation(m2, 10000);
}
fitness(m2, p2) { return -0.2; }
```

```
2000: mateChoice() {
    parent1HasMut = (individual.countOfMutationsOfType(m2) > 0);
    parent2HasMut = (sourceSubpop.individuals.countOfMutationsOfType(m2)
       > 0);
    if (parent1HasMut)
       return weights * ifelse(parent2HasMut, 2.0, 1.0);
    else
       return weights * ifelse(parent2HasMut, 0.5, 1.0);
}
3000: late() {
    sim.setValue("FST", sim.getValue("FST") + calcFST(p1, p2));
}
3499 late() {
    cat("Mean FST at equilibrium: " + (sim.getValue("FST") / 500));
    sim.simulationFinished();
}
```

This model runs very slowly after generation `2000`. The `mateChoice()` callback computes the same values over and over; using the Eidos functions `defineConstant()` and `rm()` to cache those values yields about a 10× speedup. This is left as an advanced exercise for the reader.

11.2 Sequential mate search

In the previous section we saw how to use a `mateChoice()` callback to implement assortative mating with a `mateChoice()` that modified the standard mating weights vector, `weights`, by multiplying it with an additional term derived from the genetic match between the focal individual and the other individuals in the subpopulation. In other words, the ultimate choice of mate was left to SLiM's machinery; the `mateChoice()` callback just modified the mating weights.

In this section we will explore a completely different kind of `mateChoice()` callback, one which makes the mate choice determination itself and tells SLiM's machinery which mate was chosen (if any). The standard `weights` vector will be used internally, within the `mateChoice()` callback; but the callback will return a weights vector with `1` for the chosen mate and `0` for all other candidates. In certain circumstances, it will instead return a zero-length vector as a signal to SLiM that no suitable mate could be found, initiating a new mate search with a new choosing parent.

The biological scenario here has to do with sequential mate search, the search by the choosy parent for a suitable mate by examining candidates sequentially until a suitable candidate is found or the breeding season runs out. Conceptually, we will model a species like peacocks, in which the choosy parent is looking for a mate with a large ornament that is costly in fitness but that makes the mate attractive; however, to keep the model relatively simple we will do a hermaphroditic model in which all individuals can play both the chooser and the chosen.

Let's build the model one step at a time, first constructing the genetic and population structure:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);    // neutral
    initializeMutationType("m2", 0.5, "f", -0.01);  // ornamental
    initializeGenomicElementType("g1", c(m1, m2), c(1.0, 0.01));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
2001 early() {
    sim.simulationFinished();
}
```

This is straightforward: one population of 500 individuals, and a genetic structure that allows both neutral mutations (m1) and mutations that influence the ornament size of the individuals (m2). The ornamental mutations occur only about 1% as often as the neutral mutations, but may occur anywhere in the genome; this could be thought of as a "many genes of small effect", quantitative-genetics sort of scenario. These ornamental mutations are all slightly deleterious, as genes that increase the size of a peacock's tail presumably would be (apart from their positive effect on mating). If run, this model behaves as you might expect: neutral mutations accumulate, but no ornamental mutations fix, or even reach appreciable frequency, because of their deleterious effect.

Now we want to introduce the effect of the ornamental mutations on mating; to do so, we add a mateChoice() callback. This callback should implement sequential choosy mate choice by searching for a mate, preferring potential mates with more ornamental mutations:

```
mateChoice() {
    fixedMuts = sum(sim.substitutions.mutationType == m2);
    for (attempt in 1:5)
    {
       mate = sample(0:499, 1, T, weights);
       osize = 1.0 + (fixedMuts * 0.01) - p1.cachedFitness(mate);

       if (runif(1) < osize * 10 + 0.1)
          return p1.individuals[mate];
    }
    return float(0);
}
```

The first line of this callback just totals up the number of ornamental mutations that have fixed. Once a mutation fixes, SLiM removes it from the active simulation, and from fitness calculations; since all individuals possess the fixed mutation, it has no differential effect on fitness or dynamics, in general. In this model, however, we want such fixed mutations to continue to influence mate choice, as described below. This could also be done (perhaps better) by setting the convertToSubstitution property of m2 to F, as we have seen in some previous recipes; we're using a different strategy here just to show a different angle on this common issue.

Next, the callback uses a for loop to make up to five attempts at finding a mate. Each attempt is a little less picky than the previous attempt, reflecting declining standards as breeding season proceeds. If all five attempts fail, float(0) is returned to indicate that the individual failed to find a mate. Within each attempt, a candidate mate is chosen using the sample() function, with the standard fitness-based weights vector as the weights for sampling; the deleterious effect of the ornamental mutations is thus still taken into account, reducing the likelihood that highly ornamented individuals will be chosen as mates for survival- or growth-based reasons. The ornament size of the candidate mate is calculated, using both fixed and unfixed ornamental mutations. Finally, runif() generates a random uniform draw (between 0 and 1, by default), and that drawn value is compared to a threshold value determined by the candidate mate's ornament size; if the candidate gets sufficiently lucky, it ends up as the chosen mate. (The addition of 0.1 here ensures that the mate choice algorithm is guaranteed to terminate eventually; without it, a hang would be possible if no individual can ever find a suitable mate because no individuals with any ornamental mutations exist.) When a mate is chosen, it is simply returned; it just needs to be looked up from p1.individuals since mate is just the index of the chosen mate. It would be possible instead to construct a new weights vector, with 1 for the chosen mate and 0 for all other entries, and return that to force SLiM to choose that individual; simply returning the individual is a shorthand that can be handled by SLiM far more efficiently than can a returned weights vector.

If you run this model, you can now see the ornamental mutations increasing in frequency and fixing despite their deleterious fitness effect, because they are favored by sexual selection.

We might be interested in the final ornament size attained, so we can flesh out the final event:

```
2001 early() {
    fixedMuts = sum(sim.substitutions.mutationType == m2);
    osize = 1.0 + (fixedMuts * 0.01) - mean(p1.cachedFitness(NULL));
    cat("Mean ornament size: " + osize);
    sim.simulationFinished();
}
```

By writing this as a `2001 early()` event, we are effectively running at the very end of generation `2000`, after fitness values have been evaluated (see the generation cycle diagram in section 1.3, or the more in-depth discussion in chapter 19). This distinction is important, since this event calls `cachedFitness()` to get the fitness values of individuals; in a `late()` event those values would not yet be calculated, and in fact calling `cachedFitness()` at that time would result in an error.

If you run this model until completion, you will likely see an output line like:

```
Mean ornament size: 0.0905
```

Individuals have evolved to possess, on average, about nine ornamental mutations. If you modify the model to run until generation `10001`, the final state is not much different:

```
Mean ornament size: 0.09
```

The fact that the mate choice algorithm takes fixed mutations into account, comparing the true ornament sizes of candidate mates, means that having an ornament above a certain threshold size provides no marginal benefit; indeed, because of the deleterious fitness effect of the ornamental mutations, additional ornamental mutations above that threshold are selected against. The model therefore reaches an equilibrium ornament size, just as happens in reality with ornamented species subject to both natural selection against the ornament and sexual selection for the ornament, such as peacocks. In this toy model, the equilibrium value is easily predicted from the structure of the model itself (the key predictor is the mathematics of the `runif()` comparison in the callback).

For the record, here is the full model with all of the above components:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);    // neutral
    initializeMutationType("m2", 0.5, "f", -0.01);  // ornamental
    initializeGenomicElementType("g1", c(m1, m2), c(1.0, 0.01));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
mateChoice() {
    fixedMuts = sum(sim.substitutions.mutationType == m2);
    for (attempt in 1:5)
    {
       mate = sample(0:499, 1, T, weights);
       osize = 1.0 + (fixedMuts * 0.01) - p1.cachedFitness(mate);
       
       if (runif(1) < osize * 10 + 0.1)
          return p1.individuals[mate];
    }
    return float(0);
}
```

```
2001 early() {
    fixedMuts = sum(sim.substitutions.mutationType == m2);
    osize = 1.0 + (fixedMuts * 0.01) - mean(p1.cachedFitness(NULL));
    cat("Mean ornament size: " + osize);
    sim.simulationFinished();
}
```

Any kind of preference, bias, search, benefit, or cost influencing mate choice or mating eligibility can be modeled with `mateChoice()` callbacks; this recipe only scratches the surface.

11.3 Gametophytic self-incompatibility

In the previous sections we have seen the use of `mateChoice()` callbacks to implement assortative mating and sequential mate choice, two types of non-random mating. In this section, we will see the use of a different type of callback, a `modifyChild()` callback, to model an interesting type of non-random mating, gametophytic self-incompatibility based on S-locus alleles.

Gametophytic self-incompatibility is quite a common mating scheme in plants. In a nutshell, the pollen grain (the male gamete, which is haploid) expresses the particular allele that it possesses at a special locus called the S-locus. When a pollen grain lands on the stigma of a female flower and begins to grow a pollen tube down the style towards the ovaries of the flower, the pollen tube expresses the S-locus allele of the pollen grain as it grows. Female flowers, in their styles, do some sort of check of the S-locus allele being expressed by the pollen tube, and if it exactly matches an S-locus allele possessed by the female plant (on either of its two copies of that locus, since the female flower is part of a diploid plant), it halts the growth of the pollen tube, preventing fertilization. The reasons why this mechanism might be beneficial are thought to be related to promotion of outcrossing and prevention of selfing.

Why use a `modifyChild()` callback instead of a `mateChoice()` callback to model a mate choice scheme such as gametophytic self-incompatibility? There are several considerations. Conceptually, a `mateChoice()` callback allows control over how likely every possible mating pair in a population is to form, whereas a `modifyChild()` callback is about controlling the outcome of a specific mating – governing whether that mating is fertile and what the genetic outcome of the mating is. Gametophytic self-incompatibility is not really about the choice of mates across the population (pollen lands indiscriminately on all female flowers, at least without complications such as heterostyly or enantiostyly); instead, it is about whether the combination of a specific pollen grain and a specific flower is fertile or infertile, making `modifyChild()` a natural choice.

Another consideration is that `mateChoice()` callbacks are about pre-mating reproductive isolation, whereas `modifyChild()` callbacks are about post-mating reproductive isolation (among other uses). Gametophytic self-incompatibility depends upon the S-locus allele expressed by the haploid pollen grain; that information is simply not available in a `mateChoice()` callback, since gametes have not yet been produced at that stage. From this perspective, then, `modifyChild()` is actually a forced choice for this recipe.

A third consideration is that if a `mateChoice()` callback rejects a first parent completely, SLiM's mating algorithm goes back to try a different first parent within the same source subpopulation, whereas if a `modifyChild()` callback suppresses a child completely, SLiM's mating algorithm re-chooses the source subpopulation as well, based upon the migration rates set for the target subpopulation (see section 19.2). This difference reflects the pre-mating versus post-mating semantics of the two callbacks, and makes good sense here; if a particular source subpopulation's pollen grains have a high probability of being incompatible with the female flowers of the target subpopulation, that source subpopulation should be underrepresented in gene flow into the target subpopulation, compared to the expected gene flow based upon pollen flow alone.

A final consideration, if none of the previous issues decides the question, might be speed. Unfortunately, `mateChoice()` callbacks tend to be quite slow. In computer science parlance, they are generally O(N), meaning that the computation time taken by a `mateChoice()` callback is proportional to the number of individuals in the subpopulation; this is because each individual must be evaluated to produce a mating weight. On the other hand, `modifyChild()` callbacks are generally O(1), meaning they take a constant amount of time regardless of population size; this is because only the product of one mating event is considered by the callback. In practice, this algorithmic speed difference can result in a very large difference to the running speed of a model. Usually, however, the previous considerations will dictate the choice of implementation.

Let's build the model in two steps, beginning without the `modifyChild()` callback:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "f", 0.0);  // S-locus mutations
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElementType("g2", m2, 1.0);
    initializeGenomicElement(g1, 0, 20000);
    initializeGenomicElement(g2, 20001, 21000);
    initializeGenomicElement(g1, 21001, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
10000 late() {
    cat("m1 mutation count: " + sim.countOfMutationsOfType(m1) + "\n");
    cat("m2 mutation count: " + sim.countOfMutationsOfType(m2) + "\n");
}
```

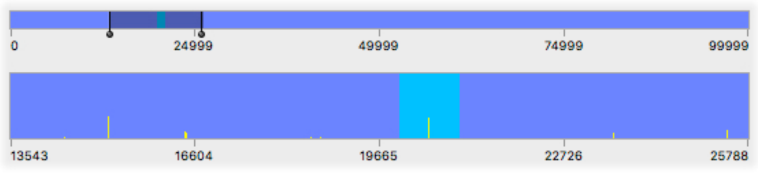
We have two mutation types, both neutral, and a chromosome that uses mutation type `m1` over most of its length (with `g1`) but mutation type `m2` within a small (`1000`-bp) locus (with `g2`). That small locus is of course the S-locus, but without the `mateChoice()` callback it acts identically to the rest of the chromosome. Since there is not yet any code to enforce a difference between the S-locus and the rest of the chromosome, this recipe is, at this point, simply a model of neutral drift.

In the generation `10000` event, it outputs two metrics prior to termination: the number of mutations of type `m1` and of type `m2`. These serve as a quick-and-dirty measure of genetic diversity, both across the bulk of the chromosome (the m1 count) and within the S-locus (the m2 count). A typical test run of this recipe produces something like:

```
m1 mutation count: 124
m2 mutation count: 1
```

You can run the model a bunch of times and confirm that there is not a whole lot of variation around these numbers; the `m1` count is typically `100`–`200`, the `m2` count typically `0`–`5`.

It is also interesting to look at the graphical representation of the chromosome in SLiMgui. Selecting a subrange of the chromosome, so as to zoom in on just one section, a typical run of the recipe so far looks like:



This view has display of genomic elements turned on, with the Ⓖ button, so that the location of the S-locus is clear. The two things to note here are that the distribution of neutral mutations is fairly sparse, and that the distribution of neutral mutations inside versus outside the S-locus is comparable.

Now let's add in the modifyChild() callback that implements the gametophytic self-incompatibility system:

```
modifyChild(p1) {
    pollenSMuts = childGenome2.mutationsOfType(m2);
    styleSMuts1 = parent1Genome1.mutationsOfType(m2);
    styleSMuts2 = parent1Genome2.mutationsOfType(m2);
    if (identical(pollenSMuts, styleSMuts1))
       if (runif(1) < 0.99)
          return F;
    if (identical(pollenSMuts, styleSMuts2))
       if (runif(1) < 0.99)
          return F;
    return T;
}
```

First, the callback gets a vector of all of the S-locus mutations present in the pollen grain. The childGenome2 variable is defined by SLiM within modifyChild() callbacks, and represents the gamete produced by the second parent in the mating; see section 22.4 for details. The result, pollenSMuts, represents the S-locus allele expressed by the pollen grain. All mutations at the S-locus are considered, in this model, to change the expressed S-allele; it would be trivial to add in the possibility of neutral mutations at the S-locus as well, by adding in a probability of type m1 mutations in genomic element type g2.

Next, the callback gets the two S-locus alleles of the female flower by fetching the vector of mutations of type m2 from parent1Genome1 and parent1Genome2, the two homologous genomes of the first parent (again, defined by SLiM in these callbacks, and documented in section 22.4).

Next comes the crucial step at which the growth of the pollen tube is stopped if there is an incompatibility between the S-allele of the pollen and either of the S-alleles of the female flower. This is checked using the Eidos function identical(), which checks whether its two arguments are exactly identical. We don't need to worry about non-identicality due to mutations being listed in a different order in the vectors, because Genome keeps its list of mutations in sorted order, and mutationsOfType() returns a sorted subset of that list.

If the pollen S-allele is identical to either of the female flower's S-alleles, there is a 99% probability (in this model) of the pollen tube being blocked, as implemented by the test (runif(1) < 0.99). Returning F in these cases tells SLiM to suppress generation of the proposed child altogether; this is, conceptually, the stoppage of the pollen tube. It is important to guarantee that a modifyChild() callback will never suppress 100% of all proposed children, for any state that your model might reach; if that ever happens, SLiM will hang, stuck in an infinite loop generating an infinite succession of proposed children that all get suppressed. In this case, the model would not quite hang without the runif() test, since eventually SLiM would manage to generate pollen grains that all happened to have a mutation within the S-locus that made them compatible with the available female flowers; but it would take an awfully long time. Indeed, even at 99% the first generation can take quite a while to finish, and many of the individuals in the second generation will have an S-locus mutation because of the effective imposition of gametophytic self-incompatibility in a single generation. A more realistic model might perhaps "phase in" the gametophytic self-incompatibility slowly over some thousands of generations, reflecting the gradual evolution of an increasingly strong mechanism, by making the threshold against which runif() is compared depend upon sim.generation. This is left as an exercise for the reader; it should not change the final state of the model at equilibrium (although equilibrium might take a lot more than the 10000 generations we use here).

The final line simply returns T, indicating that since the pollen grain was compatible with the female flower, the proposed child can be generated.

The full recipe, for the record:

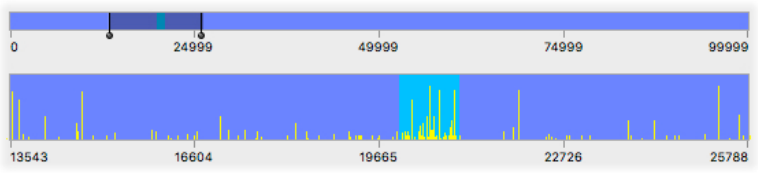
```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "f", 0.0);  // S-locus mutations
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElementType("g2", m2, 1.0);
    initializeGenomicElement(g1, 0, 20000);
    initializeGenomicElement(g2, 20001, 21000);
    initializeGenomicElement(g1, 21001, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
10000 late() {
    cat("m1 mutation count: " + sim.countOfMutationsOfType(m1) + "\n");
    cat("m2 mutation count: " + sim.countOfMutationsOfType(m2) + "\n");
}
modifyChild(p1) {
    pollenSMuts = childGenome2.mutationsOfType(m2);
    styleSMuts1 = parent1Genome1.mutationsOfType(m2);
    styleSMuts2 = parent1Genome2.mutationsOfType(m2);
    if (identical(pollenSMuts, styleSMuts1))
       if (runif(1) < 0.99)
          return F;
    if (identical(pollenSMuts, styleSMuts2))
       if (runif(1) < 0.99)
          return F;
    return T;
}
```

If you run the full recipe, you should get output something like:

```
m1 mutation count: 582
m2 mutation count: 55
```

There is vastly more genetic diversity now, both within the S-locus (mutation type m2) and across the whole chromosome (type m1). Gametophytic self-incompatibility basically imposes a regime of balancing selection (i.e., negative frequency-dependent selection) at the S-locus, and that regime tends to preserve allelic diversity at the locus (see section 9.4.1 for a different model of negative frequency-dependent selection). It also increases the outcrossing rate in the population, particularly when there are relatively few S-alleles (when there are many S-alleles, it would mostly tend to diminish selfing, since most non-selfing mating pairs would possess different S-alleles anyway; it would be trivial, of course, to add selfing to this model to experiment with that additional nuance, as seen in section 6.3.1).

Examining the same subsection of the chromosome as before, in SLiMgui, it now looks like this:



Compare this to the previous snapshot, and the increase in genetic diversity across the chromosome is immediately apparent. It is also striking how much more diversity is contained within the S-locus itself (due to the balancing selection there) compared to the rest of the chromosome. Note that in the implementation of this model, the number of S-alleles is not just the number of different mutations within the S-locus that are circulating in the population. Instead, every unique haplotype within the S-locus as a whole represents a different S-allele, and new S-alleles can be generated in this model by recombination as well as by mutation. Other schemes for evaluating what an S-allele "really" is, based upon the mutations present at the S-locus, could of course be implemented using a different test than `identical()` in the `modifyChild()` callback.

12. Direct child modifications

Thus far we have seen two ways of modifying SLiM's basic Wright-Fisher model: `fitness()` callbacks that modify the default fitness of mutations (chapter 9), and `mateChoice()` callbacks that alter the default behavior of random mating (chapter 11). In this chapter we will look at a third type of modification, `modifyChild()` callbacks. These allow you to modify children generated by SLiM (by adding or removing mutations, for example), or to suppress particular children entirely (see section 1.5 for a full technical discussion). Here, we will look at how to use a `modifyChild()` callback to solve three specific problems: social learning of cultural traits that modify fitness, lethal epistasis, and simulating a "gene drive" based upon CRISPR/Cas9. Note that section 11.3 also used a `modifyChild()` callback, to implement a gametophytic self-incompatibility system.

12.1 Social learning of cultural traits

In section 9.4.3 we explored a simple model of a cultural trait; the `tag` value of `Individual` was used to track whether each individual was a milk-drinker or not, and a `fitness()` callback was used to make mutations promoting the production of lactase into adulthood beneficial for milk-drinkers but neutral for non-milk-drinkers. In that model, whether a given individual was a milk-drinker or not was determined at random, in a `late()` callback that tagged all offspring with their assigned cultural group. We will now take up that model again and extend it to be a model of social learning: individuals will tend to inherit milk-drinking from their parents, although a substantial random factor in the cultural assignment will be retained. To achieve this, instead of assigning the cultural group in a `late()` event, we will do it in a `modifyChild()` callback, so that we have the information we need regarding the culture of the parents. The recipe:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);   // neutral
    initializeMutationType("m2", 0.5, "f", 0.1);   // lactase-promoting
    m2.convertToSubstitution = F;
    initializeGenomicElementType("g1", c(m1,m2), c(0.99,0.01));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 1000);
    p1.individuals.tag = rbinom(1000, 1, 0.5);
}
modifyChild() {
    parentCulture = (parent1.tag + parent2.tag) / 2;
    childCulture = rbinom(1, 1, 0.1 + 0.8 * parentCulture);
    child.tag = childCulture;
    return T;
}
fitness(m2) {
    if (individual.tag == 0)
       return 1.0;         // neutral for non-milk-drinkers
    else
       return relFitness;  // beneficial for milk-drinkers
}
10000 { sim.simulationFinished(); }
```

The setup of the model is similar to its predecessor in section 9.4.3: mutation type `m2` is used to represent alleles that promote retention of lactase production (and removal of fixed `m2` mutations is prevented with `convertToSubstitution`), `tag` values of `1` are used to indicate milk-drinkers, and the same `fitness()` callback as in section 9.4.3 produces a differential fitness effect of `m2` mutations depending upon the culture of the individual. What has changed is the way that the tag values are maintained. The `late()` event has been removed. We now assign initial `tag` values in generation 1, immediately after creating subpopulation `p1`. Thenceforth, the tag values of new individuals are assigned in the `modifyChild()` callback:

```
modifyChild() {
    parentCulture = (parent1.tag + parent2.tag) / 2;
    childCulture = rbinom(1, 1, 0.1 + 0.8 * parentCulture);
    child.tag = childCulture;
    return T;
}
```

This callback is called once for every new offspring individual created, throughout the run of the model. Its first line gets the `tag` values of the two parents (using `parent1` and `parent2` variables that are set up for all `modifyChild()` callbacks; see section 22.4 for a complete list of these variables), and averages them to get a `parentCulture` value that will be `0`, `0.5`, or `1`. The next line determines what the child's culture will be (`0` or `1`) using `rbinom()` to draw from a binomial distribution; the trial success probability used for the draw depends on `parentCulture` in such a way as to make children tend to follow the culture of their parents, but with a 10% chance of deviating even if the parents share the same culture. To make this cultural determination take effect, `childCulture` is assigned into the `tag` property of the child (using the `child` variable defined for the callback by SLiM). Finally, a value of `T` is returned to indicate that the child should be generated; it is possible for a `modifyChild()` callback to suppress the generation of some children by returning `F`.

In the original model of section 9.4.3, the fraction of milk-drinkers remained about `0.5`, because assignment into a cultural group was random. In this model, in contrast, the fraction of milk-drinkers can increase over time as individuals learn milk-drinking from their parents; the fitness benefit of milk-drinking increases as more `m2` mutations sweep. It is easy to observe this in SLiMgui by adding a custom output event:

```
{
    if (sim.generation % 100 == 0)
      cat(sim.generation + ": " + mean(p1.individuals.tag) + "\n");
}
```

This prints the fraction of milk-drinkers in the population, every `100` generations. Running this model produces output that shows the progressive increase in milk-drinking:

```
100: 0.465
200: 0.567
300: 0.552
400: 0.681
500: 0.735
...
```

However, there will always be a minimum of about 10% non-milk-drinkers in the population, because of the element of chance provided by the binomial draw in the `modifyChild()` callback. It would be possible to modify that to allow a specific culture to fix in the population. On the other hand, one could also model the fact that milk-drinkers who do not retain lactase production into adulthood will typically suffer from symptoms of lactose intolerance, making milk-drinking disadvantageous in some circumstances. One could also model a slight deleterious effect of lactase retention genes among non-milk-drinkers, since they are devoting energy to producing an enzyme that they do not use. There is always more complexity to be added; but as it stands, this model shows the coevolution of both genetic and cultural factors related to milk-drinking, using `tag` values in combination with a `modifyChild()` callback to model social learning in SLiM.

12.2 Lethal epistasis

In section 9.3.1 we saw a model of epistasis that influenced the fitness of the epistatic alleles using a `fitness()` callback. Sometimes the situation is simpler than the scenario presented in that model: sometimes the fitness of individuals carrying both epistatic alleles is zero, making the epistatic interaction lethal. In this case, a `modifyChild()` callback is well-suited to the task, since it can suppress the generation of particular offspring depending upon their genetics (or other factors). In this case, we will model two introduced mutations, `A` and `B`, which are normally beneficial, but are lethal when they occur in the same offspring:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "f", 0.5);  // mutation A
    m2.convertToSubstitution = F;
    initializeMutationType("m3", 0.5, "f", 0.5);  // mutation B
    m3.convertToSubstitution = F;
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
}
1 late() {
    sample(p1.genomes, 20).addNewDrawnMutation(m2, 10000);  // add A
    sample(p1.genomes, 20).addNewDrawnMutation(m3, 20000);  // add B
}
modifyChild() {
    childGenomes = c(childGenome1, childGenome2);
    hasMutA = any(childGenomes.countOfMutationsOfType(m2) > 0);
    hasMutB = any(childGenomes.countOfMutationsOfType(m3) > 0);
    if (hasMutA & hasMutB)
       return F;
    return T;
}
10000 { sim.simulationFinished(); }
```

The mechanics here for the introduction of mutations `A` and `B` follow the pattern we have seen in other recipes: a target vector of genomes is chosen with `sample()`, and then a mutation is added to the target genomes with `addNewDrawnMutation()`. Unlike most previous recipes, however, here we sample `20` genomes, not just one, in order to add the new mutation to multiple individuals. Because `addNewDrawnMutation()` is a class method of `Genome`, not an instance method, a single new mutation is added to all of the target genomes, rather than a different new mutation being added to each target genome as a result of multicasting; see section 9.4.4 for discussion of the mechanics of this. No effort is made here to avoid adding `A` and `B` to the same individuals, but that would be trivial to add by refining the choice of targets for `B`. The mutation types for `A` and `B`, `m2` and `m3`, are set not to convert fixed mutations to substitutions, so that their epistatic interaction persists even after fixation; see section 9.3.1 for extensive discussion of this.

The new and interesting behavior is in the `modifyChild()` callback. First it determines whether the proposed child possesses mutation `A` and mutation `B`, setting up logical flags `hasMutA` and hasMutB by checking whether the count of mutations of the relevant type is greater than zero in either of the child's genomes. Then, if the child has both A and B, it returns F, indicating that this child should be suppressed. New parents will be chosen and a new child will be generated instead (also subject to the approval of the modifyChild() callback). Otherwise it returns T, indicating the generation of the child should proceed.

When this model is run, either A or B quickly "wins", fixing while its epistatic competitor is lost. If the modifyChild() callback is removed, on the other hand, both A and B will typically fix. We can try an interesting variant by making the epistatic interaction lethal only if A and B are both homozygous, by replacing the previous modifyChild() callback with a new version:

```
modifyChild() {
    childGenomes = c(childGenome1, childGenome2);
    mutACount = sum(childGenomes.countOfMutationsOfType(m2));
    mutBCount = sum(childGenomes.countOfMutationsOfType(m3));
    if ((mutACount == 2) & (mutBCount == 2))
       return F;
    return T;
}
```

This results in a form of balancing selection between A and B, since now homozygosity is disadvantageous but heterozygosity is advantageous. Both will tend to fluctuate around a frequency of 0.5, although one may stochastically manage to fix eventually (in which case the other will immediately be lost).

This type of model could also be used to represent an epistatic interaction during development that is lethal in some fraction of cases, but is otherwise harmless – either the epistatic interaction causes a lethal anomaly during development, or it doesn't, in which case the offspring is normal. This could be modeled simply by adding a random factor to the if statement in the modifyChild() callback.

12.3 Simulating gene drive

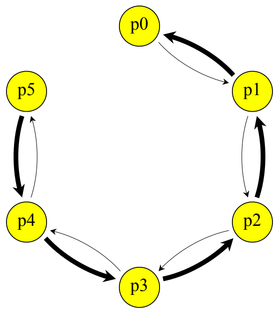
There has recently been a lot of buzz about a new genetic-engineering technology called CRISPER/Cas9 that allows genetic modifications to be performed much more quickly and easily than previous methods (Doudna & Charpentier 2014). One potential application of the CRISPER/Cas9 machinery is to use it for the construction of a so-called *gene drive*, which can quickly drive genetically modified alleles to high frequency in a population even if they carry a fitness cost. We will here refer to a CRISPR/Cas9-based gene drive with the term mutagenic chain reaction, or MCR.

The basic idea of MCR is that the CRISPR/Cas9 machinery embedded into the organism's genome could cause the machinery itself to be spliced into any homologous chromosome that does not already contain it. If a fertilized egg ends up with one copy of the MCR machinery, inherited from one parent, the machinery could then splice itself into the homologous chromosome in the egg, changing the egg from being heterozygous to homozygous for the MCR locus. This is in some ways similar to the idea of meiotic drive and related concepts in evolutionary biology, and it clearly underlines the fundamental truth of the "selfish gene" perspective: an MCR gene of this type could, as we shall see, spread to fixation in a population even if it has a deleterious fitness effect at the level of the individual organism.

Just for fun, we're going to make this model relatively complex in terms of population structure, and we're going to introduce spatial variation in selection using a fitness() callback as well. We'll build this model one step at a time, starting with the demographic structure:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);   // neutral
    initializeMutationType("m2", 0.5, "f", -0.1);  // MCR complex
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    for (i in 0:5)
       sim.addSubpop(i, 500);
    for (i in 1:5)
       sim.subpopulations[i].setMigrationRates(i-1, 0.001);
    for (i in 0:4)
       sim.subpopulations[i].setMigrationRates(i+1, 0.1);
}
10000 { sim.simulationFinished(); }
```

This sets up a six-subpopulation stepping-stone model, similar to that previously discussed in section 5.3.1. Note that migration in this model is primarily from p5 down to p0; the migration rate in that direction is a hundred times higher than in the direction from p0 up to p5:



The code above sets up a mutation type m2 for the MCR complex, but doesn't use it, so at present this is just a simulation of neutral drift in a stepping-stone model. Let's start using mutation type m2, although not yet with its planned MCR capabilities, by adding a little code to introduce an m2 mutation and track its fate (the tracking block can replace the final script block in the previous model):

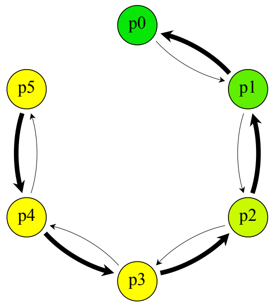
```
100 late() {
    p0.genomes[0:49].addNewDrawnMutation(m2, 10000);
}
100:10000 late() {
    if (sim.countOfMutationsOfType(m2) == 0)
    {
       fixed = any(sim.substitutions.mutationType == m2);
       cat(ifelse(fixed, "FIXED\n", "LOST\n"));
       sim.simulationFinished();
    }
}
```

The introduction code here simply introduces the mutation into the first 50 genomes of subpopulation p0, without bothering to randomly select target individuals using sample(). Introducing the mutation into many genomes at once is a quick-and-dirty trick to help an introduced mutation avoid being lost due to genetic drift at the earliest stages of establishment, without putting in the machinery to make the simulation truly conditional on establishment as we did in section 10.3. Biologically, it could be viewed as a large-scale immigration event, or as a planned introduction of mutant individuals orchestrated by humans. See section 9.4.4 for discussion of the Eidos mechanics underlying this mutation introduction code.

This model will generally terminate, perhaps around generation `140`, with the message `"LOST"`. This is because mutation type `m2` is strongly deleterious, as presently defined, and so gets eliminated by selection fairly quickly even though it is initially introduced in fifty copies. Since this is not very interesting, let's move on to the next step: making mutation type `m2` strongly beneficial in subpopulation `p0` and strongly deleterious in subpopulation `p5`, with gradations in between, using a `fitness()` callback:

```
fitness(m2) {
    return 1.5 - subpop.id * 0.15;
}
```

This `fitness()` callback uses `subpop.id`, the identifier of the subpopulation in which the mutation is presently being evaluated, to generate a fitness of `1.5` for `p0`, but a fitness of `0.75` for `p5`. If we run the model now, we see that it soon reaches an equilibrium state of migration-selection balance:



It is at high frequency in `p0` – nearly fixed, but prevented from fixing completely by gene flow from `p1`. It is essentially absent from `p5`, on the other hand, since it is weeded out by selection, and since gene flow in the `p0` to `p5` direction is so weak. The model will tend to maintain this dynamic equilibrium.

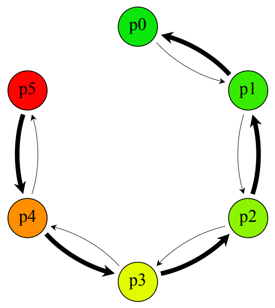
Let's add the `modifyChild()` callback that implements the MCR behavior of `m2`:

```
100:10000 modifyChild() {
    mut = sim.mutationsOfType(m2);
    if (size(mut) == 1)
    {
       hasMutOnChromosome1 = childGenome1.containsMutations(mut);
       hasMutOnChromosome2 = childGenome2.containsMutations(mut);
       if (hasMutOnChromosome1 & !hasMutOnChromosome2)
          childGenome2.addMutations(mut);
       else if (hasMutOnChromosome2 & !hasMutOnChromosome1)
          childGenome1.addMutations(mut);
    }
    return T;
}
```

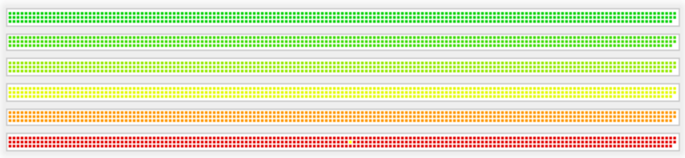
The first line just finds the introduced mutation by searching for it in the list of mutations kept by the simulation; this is necessary because SLiM and Eidos don't allow you to keep permanent references to objects. The `if` statement tests whether we found the MCR mutation; in the final generation of the simulation, when the mutation has either fixed or been lost, we won't find it.

Assuming we do find the MCR mutation, we then check whether the particular child that we are working with – the target of this `modifyChild()` operation – has the MCR mutation in either of its genomes, using the `containsMutations()` method of `Genome`. With that information, the rest is simple: if it is in one genome but not the other, we add the MCR mutation to the genome that doesn't already contain it, just as the CRISPR/Cas9 gene drive machinery for MCR would do in an actual organism. If neither genome of the target contains the MCR gene, or if both genomes do, we leave the child as it is. Finally, we return `T`, indicating that the child in question should in fact be generated (a return of `F` would suppress generation; we saw an example of this in section 12.2).

If we recycle and run this model, it shows a consistent behavior of rapid fixation, even in the subpopulations where it is deleterious, and even despite having to "swim upstream" against the predominant direction of gene flow. At the moment just prior to complete fixation, the model looks something like this (note that once the mutation actually fixes, it is removed from the simulation and replaced by a substitution object, so the populations revert to yellow):

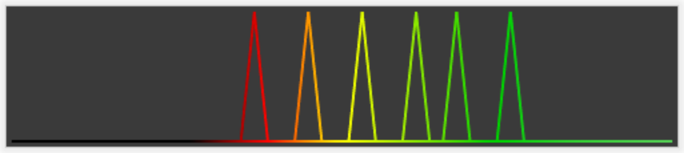


Incidentally, in snapshots like the one above, we've been using the Population Visualization graph to see the state of the model, because it is a bit more informative than the default population view, which doesn't show population connectivity:



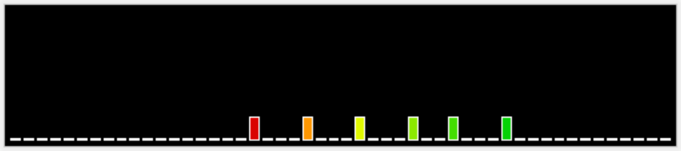
This display shows every individual in the model, colored according to its fitness. There are two other display modes for the population view that can be useful, both of which summarize that fitness distribution by binning the individual fitness values. These alternative display modes can be selected with a right-click or control-click on the population view.

One alternative is to see line plots of binned fitness for each subpopulation, superimposed:



The *x*-axis represents fitness (from 0.0 to 2.0 in this case, but this is configurable in the options panel that appears when this display mode is chosen). Fitness values are tallied into 50 bins (also configurable), and the *y*-axis represents the frequency within each bin, from 0.0 to 1.0 within each subpopulation. For this model, the resulting plot looks a bit like modern art, but the six peaks correspond to the six subpopulations; the different fitness effects in the different subpopulations is clearly visible, as is the fact that the mutation is about to fix.

Another possibility is to see a histogram of binned fitness values across all of the subpopulations. This is similar to the line plot of fitness frequencies above, except that all of the subpopulations are tallied together, not individually:



Again the *x*-axis represents fitness and the *y*-axis represents frequency within a bin (now from 0.0 to 1.0 population-wide). The six subpopulations can again be seen here.

These alternative population visualizations can be a useful tool in understanding model dynamics, especially for models with many subpopulations and/or many individuals.

For reference, here is the full gene drive model with all of the components introduced above:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);   // neutral
    initializeMutationType("m2", 0.5, "f", -0.1);  // MCR complex
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    for (i in 0:5)
      sim.addSubpop(i, 500);
    for (i in 1:5)
      sim.subpopulations[i].setMigrationRates(i-1, 0.001);
    for (i in 0:4)
      sim.subpopulations[i].setMigrationRates(i+1, 0.1);
}
100 late() {
    p0.genomes[0:49].addNewDrawnMutation(m2, 10000);
}
100:10000 late() {
    if (sim.countOfMutationsOfType(m2) == 0) {
      fixed = any(sim.substitutions.mutationType == m2);
      cat(ifelse(fixed, "FIXED\n", "LOST\n"));
      sim.simulationFinished();
    }
}
fitness(m2) {
    return 1.5 - subpop.id * 0.15;
}
100:10000 modifyChild() {
    mut = sim.mutationsOfType(m2);
    if (size(mut) == 1) {
      hasMutOnChromosome1 = childGenome1.containsMutations(mut);
      hasMutOnChromosome2 = childGenome2.containsMutations(mut);
      if (hasMutOnChromosome1 & !hasMutOnChromosome2)
        childGenome2.addMutations(mut);
      else if (hasMutOnChromosome2 & !hasMutOnChromosome1)
        childGenome1.addMutations(mut);
    }
    return T;
}
```

It has been proposed that MCR could have many compelling applications, such as driving particular mosquito species – those that carry important human diseases such as malaria – toward extinction, or at least driving a potentially deleterious gene for resistance to diseases like malaria toward fixation in those mosquito species. To know whether such proposals are realistic, however, we need to model them. In this section we developed a simple toy model of MCR; a model useful for real-world prediction would need many additional ramifications, of course, but this is a starting point for further exploration.

12.4 Suppressing hermaphroditic selfing

In section 6.3.1, it was noted that a low rate of selfing will normally be observed in SLiM in hermaphroditic models, even when the selfing rate is explicitly set to zero. This occurs because SLiM chooses each of the parents in a biparental mating randomly (weighted according to fitness), and does not explicitly prevent the same individual from being chosen as both parents. Normally this does not present a problem; it is typically a very small effect, and indeed it is sometimes desirable since the model will then better match the predictions from some simple analytical models. Sometimes, however, this selfing does prove to be an issue (particularly with small effective population sizes or high variance in fitness). In such cases, it can be prevented with a call at the beginning of the `initialize()` callback of your script:

```
initializeSLiMOptions(preventIncidentalSelfing=T);
```

Before this option was added to SLiM, preventing incidental selfing required a simple `modifyChild()` callback, illustrated by this section's recipe. This recipe is now obsolete, since it has been superseded by the configuration flag shown above; but it has been retained in the cookbook as an illustration of how `modifyChild()` callbacks can be used to perform simple changes to mating behavior of this sort. The original, now-obsolete recipe used this callback:

```
modifyChild()
{
    // prevent hermaphroditic selfing
    if (parent1 == parent2)
       return F;
    return T;
}
```

This can simply be dropped in to more or less any hermaphroditic model, such as this:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
2000 late() { sim.outputFixedMutations(); }
```

It will then suppress the selfing events, by returning `F` (and thus suppressing the proposed child) whenever the two parents of the proposed child are the same. This could be implemented as a `mateChoice()` callback instead, by changing the weight for the already-chosen first parent to `0`, but that would be much slower since a modified mating-weights vector would have to be built for each mating event. Often, as here, suppressing specific mating combinations is most easily and efficiently done with a `modifyChild()` callback instead.

There are two caveats. The first is that if you turn selfing on in your model this `modifyChild()` callback will then cause your model to hang, because SLiM will keep trying to satisfy your requested selfing rate, whereas the callback will keep preventing it from doing so. If you need to attain exactly the requested selfing rate, however, while suppressing the background selfing events generated randomly by SLiM, you can just add a check of the `isSelfing` flag provided to the `modifyChild()` callback (see section 22.4). For selfing events that are intended by SLiM to satisfy the requested selfing rate, this flag will be `T`; for any additional background selfing events caused by random mate choice, this flag will be `F`. Suppressing only the selfing events in which `isSelfing` is `F` ought to produce the desired effect. (You could also do a bit of math and set an adjusted selfing rate that accounts for the background selfing rate, but that is perhaps more error-prone.)

The other caveat is that if you define other `modifyChild()` callbacks as well, you might want to think about how the multiple callbacks will stack together. Typically you would want this selfing-suppression callback to occur first in the chain, and thus you would want to define it earliest in your script. See section 22.8 for discussion of this issue.

13. Advanced models

This chapter will present some advanced models that draw upon many of the concepts covered in previous chapters, while also using relatively advanced features of Eidos and SLiM that may not have been covered in previous recipes. A knowledge of the topics covered in previous chapters will be assumed, and simple details will not be explained in depth, to keep things short.

13.1 Quantitative genetics and phenotypically-based fitness

In this recipe we will explore a quantitative genetics model in which a phenotypic trait is based upon multiple loci with additive effects. In some respects this is similar to the model of polygenic selection developed in section 9.3.2; however, this model goes much further, explicitly modeling the phenotypic effect of the quantitative trait and producing a fitness effect based upon that phenotype. This recipe will model a trait based on 10 quantitative trait loci (QTLs), each of which can have a value of either −1 or +1; this is a common design for models of quantitative traits, but the model does not strongly depend upon this choice. (For a quantitative genetics model that uses QTLs with continuous effects and incorporates heritability, see section 13.10.)

This model also incorporates two-subpopulation structure, with limited gene flow between the subpopulations. The two subpopulations experience different environments that are selecting for different optima; unlike the model in section 9.2, however, the two environments are selecting for different phenotypes, as determined by all of the loci underlying the trait, rather than just exerting differential selection on each individual locus.

This model also includes assortative mating. Unlike the model of section 11.1, where mating was assortative based upon possession of a single introduced mutation, here mating is assortative based upon the phenotype produced by all the underlying loci. This means that mating can actually be disassortative at the genetic level, because individuals with the same phenotype might achieve that phenotype through entirely different QTLs alleles.

The genetic structure used here simulates ten separate chromosomes, with one QTL on each chromosome. SLiM simulates only one `Chromosome` object, but since the recombination map can be specified arbitrarily, a recombination rate of `0.5` between specific pairs of bases can be used to effectively subdivide that `Chromosome` object into separate chromosomes that have no linkage between them. This model places each QTL at the center of its chromosome, with `1000` bases on each side experiencing neutral mutations, but those choices are easily changed.

Finally, relatively complex custom output code in this model assesses and prints information about the genetic structure and fitness of each subpopulation at the beginning and end of the simulation, illustrating how SLiM's output can be customized.

We will start with the initialization portion of this model's script:

```
initialize() {
    initializeMutationRate(1e-5);

    // neutral mutations in non-coding regions
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);

    // mutations representing alleles in QTLs
    scriptForQTLs = "if (runif(1) < 0.5) -1; else 1;";
    initializeMutationType("m2", 0.5, "s", scriptForQTLs);
    initializeGenomicElementType("g2", m2, 1.0);
    m2.convertToSubstitution = F;
    m2.mutationStackPolicy = "l";
```

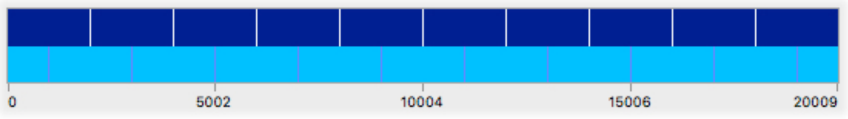
```
        // set up our chromosome: 10 QTLs, surrounded by neutral regions
        defineConstant("C", 10);    // number of QTLs
        defineConstant("W", 1000);  // size of neutral buffer on each side
        pos = 0;
        q = NULL;

        for (i in 1:C)
        {
           initializeGenomicElement(g1, pos, pos + W-1);
           pos = pos + W;

           initializeGenomicElement(g2, pos, pos);
           q = c(q, pos);
           pos = pos + 1;

           initializeGenomicElement(g1, pos, pos + W-1);
           pos = pos + W;
        }

        defineConstant("Q", q);     // remember our QTL positions

        // we want the QTLs to be unlinked; build a recombination map for that
        rates = c(rep(c(1e-8, 0.5), C-1), 1e-8);
        ends = (repEach(Q + W, 2) + rep(c(0,1), C))[0:(C*2 - 2)];
        initializeRecombinationRate(rates, ends);
    }
```

This sets up two mutation types: `m1`, representing neutral mutations, and `m2`, representing mutations at QTLs. The `m2` mutation type draws its mutational effects from a user-specified distribution, rather than from one of SLiM's built-in mutational distributions. It does this by specifying the mutation type as `"s"`, for "script", and then supplying a short Eidos snippet as a `string`. That snippet is run as a lambda (see section 17.5) by SLiM whenever it needs to draw a new selection coefficient. The `m2` mutation type is also set not to be removed when it fixes (because QTLs will continue to influence phenotype, and thus relative fitness, even after fixation); and it is set to use a "last mutation" stacking policy, so that when a new mutation occurs at a given QTL it replaces the allele that was previously at that site, rather than "stacking" with it as is SLiM's default behavior.

Two genomic element types are also set up by this code: `g1`, representing neutral buffer zones around the QTLs, and `g2`, representing QTLs themselves. The rest of this `initialize()` callback sets up the chromosome by tiling these genomic element types, and setting up a recombination map that effectively places each QTL on an independent chromosome as explained above.

This model makes somewhat liberal use of the `defineConstant()` call of Eidos to set up constants related to the genomic structure of the simulation. Defined constants are much like variables, except that they cannot be redefined (except by removing them with `rm()` first), and they persist for the lifetime of the simulation rather than disappearing at the end of the callback in which they are defined. They are thus very useful for symbolically representing model parameters; this model also defines a constant `Q` to remember the positions of all of the QTLs being simulated.

After this `initialization()` callback has run, the genetic structure of the simulation looks like this in SLiMgui (with display of genomic elements and recombination rates enabled):



This shows the pattern of non-coding regions and QTLs (below), and the recombination breakpoints that define the breaks between effective chromosomes in the model (above).

Next we will set up (most of) the initial population state of the simulation:

```
1 early() {
    sim.addSubpop("p1", 500);
    sim.addSubpop("p2", 500);
    
    // set up migration; comment these out for zero gene flow
    p1.setMigrationRates(p2, 0.01);
    p2.setMigrationRates(p1, 0.01);
    
    sim.registerEarlyEvent("s2", s1.source, 2, 2);
}
1 late() {
    // optional: give m2 mutations to everyone, as standing variation
    // if this is commented out, QTLs effectively start as 0
    g = sim.subpopulations.genomes;
    n = size(g);
    
    for (q in Q)
    {
      isPlus = asLogical(rbinom(n, 1, 0.5));
      g[isPlus].addNewMutation(m2, 1.0, q);
      g[!isPlus].addNewMutation(m2, -1.0, q);
    }
}
```

The `early()` callback sets up two subpopulations with migration between them. It also contains a call to `registerEarlyEvent()` that will not run right now; if you want to run the model at this stage you will need to comment that out. It will be explained below.

The `late()` callback is optional, and sets up the initial state of the QTLs in the model by placing initial mutations in them. It does this by looping over all of the QTLs, and for each QTL, deciding whether each genome in the simulation will start with a + or a – allele by drawing from a binomial distribution. It then distributes the + and – alleles to all of the genomes by calling `addNewMutation()` to add the chosen allele to each genome, in a twist on the pattern seen previously in section 9.4.4 and elsewhere. This code results in just two mutation objects being created to represent the + and – alleles of each QTL, rather than a different mutation object being created for each genome, for reasons explained in detail in section 9.4.4; here this is a non-essential detail, but it improves the efficiency of the model since fewer mutation objects need to be tracked. This whole callback can be removed, in which case the model starts with no QTL mutations, producing an effective value of zero for each QTL until new mutations arise. That would be a model of emerging genetic diversity from a clonal population, then, rather than this model of selection beginning with a high degree of random standing genetic variation.

Next comes a bunch of callbacks that implement the quantitative trait machinery:

```
1: late() {
    // construct phenotypes for the additive effects of QTLs
    inds = sim.subpopulations.individuals;
    inds.tag = asInteger(inds.sumOfMutationsOfType(m2));
}
fitness(m2) {
    // the QTLs themselves are neutral; their effect is handled below
    return 1.0;
}
```

```
fitness(NULL, p1) {
    // optimum of +10
    return 1.0 + dnorm(10.0 - individual.tag, 0.0, 5.0);
}
fitness(NULL, p2) {
    // optimum of -10
    return 1.0 + dnorm(-10.0 - individual.tag, 0.0, 5.0);
}
```

The `late()` callback is called in every generation to calculate the phenotypes of individuals by summing up the additive effects of all QTLs possessed by each individual. We get a vector containing all individuals in the model, and for each individual we sum up the selection coefficients of all of the `m2` mutations possessed by that individual using `sumOfMutationsOfType()` method, and place the sums into the individuals' `tag` properties with a vectorized assignment.

Note that this code would work with QTLs of any effect size, not just the +/– scheme used here, *except* that the individual's `tag` property is of type `integer`, which would lead to roundoff problems with QTLs of fractional value. That could be avoided by using the `tagF` property, which stores `float` values instead of `integer` values. Once that change was made, across the whole recipe, the phenotype values would then be saved and retrieved as type `float`, so the distribution of fitness effects could then be changed to any DFE desired (see section 13.10). This recipe uses a +/– DFE and `integer` phenotypes, partly because that is common in theoretical multilocus models, and partly for historical reasons. One could also use the `getValue()` and `setValue()` methods of `Individual` to keep the phenotype state, rather than using `tag` or `tagF` (see section 21.6.2). In other words, where this recipe saves away the calculated phenotypic value of an individual with `individual.tag = ...`, one would use `individual.setValue("phenotype", ...)` instead, and everywhere that this recipe gets a saved phenotypic value using `individual.tag`, one would use `individual.getValue("phenotype")` instead. (The `string` identifier `"phenotype"` is not special; it could just as well be `"foo"`.) This would, however, be substantially slower than using `tagF`.

The first `fitness()` callback simply makes all `m2` mutations neutral, regardless of their stated selection coefficient. This is because we are using the selection coefficients of `m2` mutations here to represent their phenotypic effect size, in the sense of additive quantitative genetics, rather than their actual selection coefficients; we therefore wish to disable their direct effect on fitness.

Finally, we have a pair of `fitness()` callbacks declared with a mutation type identifier of `NULL`: one for subpopulation `p1`, one for `p2`. We haven't seen this use of `fitness()` callbacks before; the `NULL` identifier indicates that the callback is not intended to modify the fitness effects of mutations of a particular mutation type, but rather, provides a fitness effect for the individual as a whole. For this reason, `fitness(NULL)` callbacks are referred to as global fitness callbacks (see section 22.2). They are called once for each individual in the specified subpopulation, and the fitness effect they return is multiplied into all of the other fitness effects for the individual. The fitness effect of a global `fitness()` callback might depend upon any state of the individual; here it depends on the phenotype of the individual compared to the phenotypic optimum. Since `m1` and `m2` mutations are all neutral in this model, these `fitness(NULL)` callbacks are the sole determinants of individual fitness in this model. They implement fitness based on a Gaussian fitness function, as is typical in models of this sort, with fitness being highest at some phenotypic optimum, and falling away for phenotypic values both lower and higher than that optimum. The phenotypic values of individuals are fetched out of their `tag` properties, which were set up by the `late()` event that ran previously. Note that a baseline of `1.0` is added to the Gaussian value since `1.0` indicates neutrality on the relative fitness scale; see section 13.10 for further discussion of this choice.

This implements the bulk of the model. We will now add assortative mate choice based on phenotype, which is very simple since the underlying machinery has already been constructed:

```
mateChoice() {
    phenotype = asFloat(individual.tag);
    others = asFloat(sourceSubpop.individuals.tag);
    return weights * dnorm(others, phenotype, 5.0);
}
```

This multiplicatively combines the existing fitness-based weights for all potential mates with mating weights based on a Gaussian function that rewards phenotypic similarity.

Incidentally, it might be of interest to note that now the quantitative trait is something resembling a magic trait, since it is under divergent ecological selection and influences mate choice. However, it is not in fact a magic trait, since it is based upon multiple loci. The individual QTLs might be considered "magic genes" since they perhaps satisfy the criteria of the formal definition (Servedio et al. 2011), but since there is epistasis between them (because of the way they combine additively to determine the quantitative phenotype that is actually under selection), it is not entirely clear how they relate to the usual intuitive meaning of "magic trait".

Finally, we will add some custom output by tallying up fitnesses, phenotypes, and frequencies:

```
s1 2001 early() {
    cat("-------------------------------\n");
    cat("Output for end of generation " + (sim.generation - 1) + ":\n\n");

    // Output population fitness values
    cat("p1 mean fitness = " + mean(p1.cachedFitness(NULL)) + "\n");
    cat("p2 mean fitness = " + mean(p2.cachedFitness(NULL)) + "\n");

    // Output population additive QTL-based phenotypes
    cat("p1 mean phenotype = " + mean(p1.individuals.tag) + "\n");
    cat("p2 mean phenotype = " + mean(p2.individuals.tag) + "\n");

    // Output frequencies of +1/-1 alleles at the QTLs
    muts = sim.mutationsOfType(m2);
    plus = muts[muts.selectionCoeff == 1.0];
    minus = muts[muts.selectionCoeff == -1.0];

    cat("\nOverall frequencies:\n\n");
    for (q in Q)
    {
       qPlus = plus[plus.position == q];
       qMinus = minus[minus.position == q];
       pf = sum(sim.mutationFrequencies(NULL, qPlus));
       mf = sum(sim.mutationFrequencies(NULL, qMinus));
       pf1 = sum(sim.mutationFrequencies(p1, qPlus));
       mf1 = sum(sim.mutationFrequencies(p1, qMinus));
       pf2 = sum(sim.mutationFrequencies(p2, qPlus));
       mf2 = sum(sim.mutationFrequencies(p2, qMinus));

       cat("   QTL " + q + ": f(+) == " + pf + ", f(-) == " + mf + "\n");
       cat("         in p1: f(+) == " + pf1 + ", f(-) == " + mf1 + "\n");
       cat("         in p2: f(+) == " + pf2 + ", f(-) == " + mf2 + "\n\n");
    }
}
```

This runs at the beginning of generation `2001`, so as to produce output regarding the very end of generation `2000`, after fitness values have been calculated; calling `cachedFitness()` in a `late()` event in generation `2000` would raise an error, since fitness values are not yet available at that point in the generation cycle. Note that the purpose is now clear of the line we saw before:

```
    sim.registerEarlyEvent("s2", s1.source, 2, 2);
```

This output callback is script block `s1`, which that line of code replicates as an `early()` event in generation `2`, so that it produces output at both the beginning and the end of the model run. If SLiM's syntax for specifying the generations in which a callback runs were more general, this trick would not be needed; but there is no way to say "run this callback only in generations `2` and `2001`", at present, so this is a simple way to achieve that.

Running this model produces output something like this:

```
Output for generation 1:

p1 mean fitness = 1.02108
p2 mean fitness = 1.0219
p1 mean phenotype (optimum +10) = 0.176
p2 mean phenotype (optimum -10) = -0.34

Overall frequencies:

   QTL at 1000: f(+) == 0.5125, f(-) == 0.4875
         in p1: f(+) == 0.527, f(-) == 0.473
         in p2: f(+) == 0.498, f(-) == 0.502
...
-------------------------------
Output for generation 2000:

p1 mean fitness = 1.06406
p2 mean fitness = 1.06221
p1 mean phenotype (optimum +10) = 8.296
p2 mean phenotype (optimum -10) = -8.14

Overall frequencies:

   QTL at 1000: f(+) == 0.504, f(-) == 0.496
         in p1: f(+) == 0.848, f(-) == 0.152
         in p2: f(+) == 0.16, f(-) == 0.84
...
```

It can be seen that in the initial state of the model both subpopulations have phenotypes near `0.0`, fitnesses of essentially `1.0`, and a random distribution of + and – QTL alleles. In the final state, on the other hand, phenotypes have diverged most of the way to their local environmental optima of `+10` and `-10`, mean relative fitness is up to about `1.06` in both subpopulations as a result, and substantial divergence at the level of individual QTL alleles can be observed. This divergence appears to be substantially due to the assortative mating in the model, since a sample run with the `mateChoice()` callback commented out results in considerably less divergence:

```
p1 mean fitness = 1.04107
p2 mean fitness = 1.04752
p1 mean phenotype (optimum +10) = 3.876
p2 mean phenotype (optimum -10) = -5.584
```

Of course lots of replicate runs with different parameter values, etc., would be needed to substantiate this; but it seems to agree with other models of assortative mating and divergence.

This model includes neutral diversity at loci surrounding each QTL; no attempt has been made to analyze that here, but presumably there might be interesting patterns related to patterns of gene flow, hitchhiking, and so forth. Increasing the length of the neutral buffers around the QTL (defined constant W), and/or increasing the recombination rate, would probably be helpful for making these patterns more clear.

Section 13.10 presents a fairly different quantitative genetics model, using QTLs with effect sizes drawn from a continuous distribution, and incorporating heritability, but with only a single subpopulation, with no predetermined genetic structure, and without assortative mating.

13.2 Relatedness, inbreeding, and heterozygosity

Inbreeding is an important concept in evolutionary biology, but it is not very precisely defined. It can result from a variety of processes, from small population size to assortative mating, and it can manifest in a variety of genetic patterns, such as decreased heterozygosity, loss of genetic diversity, and a decreased time to the most recent common ancestor of pairs of individuals. The particular effects of inbreeding observed in a system may depend on the process generating the inbreeding. So before embarking on a study of inbreeding, one should define one's terms clearly.

Here, we will construct a model of inbreeding that results from a tendency of individuals to mate with their close kin, as defined by their pedigree-based relatedness. SLiM (beginning in version 2.1) has a built-in facility for tracking this type of relatedness, which can be turned on with the call `initializeSLiMOptions(keepPedigrees=T)` in the `initialize()` callback of a script (see section 21.1). When this call is made, individuals in a simulation will keep track of the identities of their parents and grandparents, and the relatedness between individuals can then be assessed using the `relatedness()` method of `Individual` (see section 21.6.2). The pedigree information is also available through properties on the Individual class (section 21.6.1), for purposes such as locating "trios" (two parents and an offspring that they generated) for analysis.

It should be emphasized that the relatedness metric available through this mechanism is purely pedigree-based. This can be quite different from genetic relatedness, which depends not only on pedigree but also on factors such as assortment and recombination (see section 13.9). The inbreeding generated by this model will be based upon this relatedness metric.

With that as preamble, here is the first stage of the model:

```
initialize() {
    initializeSLiMOptions(keepPedigrees = T);
    initializeMutationRate(1e-5);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-7);
}
1 {
    sim.addSubpop("p1", 100);
}
1000 late() {
    // Calculate mean nucleotide heterozygosity across the population
    total = 0.0;

    for (ind in p1.individuals)
    {
       // Calculate the nucleotide heterozygosity of this individual
       muts0 = ind.genomes[0].mutations;
       muts1 = ind.genomes[1].mutations;

       // Count the shared mutations
       shared_count = sum(match(muts0, muts1) >= 0);
```

```
            // All remaining mutations are unshared (i.e. heterozygous)
            unshared_count = muts0.size() + muts1.size() - 2 * shared_count;

            // pi is the mean heterozygosity across the chromosome
            pi_ind = unshared_count / (sim.chromosome.lastPosition + 1);
            total = total + pi_ind;
        }

        pi = total / p1.individuals.size();

        cat("Mean nucleotide heterozygosity = " + pi + "\n");
    }
```

This is a simple neutral model, similar to those we have seen before. It turns on pedigree tracking in its `initialize()` callback, and then runs for `1000` generations. At the end of the run, a `late()` callback computes the mean nucleotide heterozygosity (π) across the population. For one individual, the nucleotide heterozygosity is the fraction of base positions that are heterozygous. This is calculated by getting the mutations from the two genomes of the individual and finding the number of mutations that are shared between them (adding the number of matches from `match()` with `sum()`). The two genomes must together contain `2 * shared_count` of these shared mutations; all the remaining mutations in the genomes are unshared, and thus heterozygous. Dividing the number of unshared mutations by the length of the chromosome (`+1` because `lastPosition` is a zero-based value) yields the individual's nucleotide heterozygosity. (Note that reuseable functions to calculate heterozygosity are now in the SLiM-Extras repository online, too, with a different implementation using `setSymmetricDifference()`; for now, this recipe doesn't use that code.)

So now we have a baseline model that has only whatever inbreeding results from its small population size of `100` individuals. Now let's add a `mateChoice()` callback that uses the pedigree tracking information to create a mating preference for kin:

```
    mateChoice() {
        // Prefer relatives as mates
        return weights * (individual.relatedness(sourceSubpop.individuals) +
          0.01);
    }
```

This uses the `relatedness()` method of `Individual` to calculate the relatedness between the focal individual that is choosing a mate (`individual`) and all of its potential mates (`sourceSubpop.individuals`). A constant of `0.01` is added to those values to guard against the possibility that all of the values would be exactly zero; that would result in a weights vector of all zeros being returned to SLiM, which is illegal (see the discussion in section 22.3). In fact, this particular model is safe from that problem, because the relatedness of an individual to itself is `1.0`, and so individuals will always be able to mate with themselves; but the safeguard is shown here to raise awareness of the issue, since in many other types of models this issue will need to be considered – sexual models, models with multiple subpopulations and migration, etc. Finally, the relatedness values are multiplied by `weights`, the vector of default mating weights supplied to the callback by SLiM. Again, this is not important for this model (as a neutral, non-sexual model, `weights` will be a vector of all `1`), but it is important for models more generally, so that the fitness-based mating weights are taken into account even when a `mateChoice()` callback is implemented. Without this, the fitness-based mating weights computed by SLiM would be completely replaced by the `mateChoice()` callback, making all selection coefficients and `fitness()` callbacks irrelevant – rarely what is wanted.

This particular callback makes the mating weights be (almost) proportional to relatedness. Individuals that share no grandparents will have a mating weight of only `0.01`, whereas full siblings will have a weight of `0.51` and an individual will have a weight of `1.01` for hermaphroditic selfing. This should generate fairly strong inbreeding. Of course a `mateChoice()` callback could rescale or otherwise modify these values to produce whatever mating preferences are desired.

That's all of the code needed for the model; the bulk of the code is actually the heterozygosity calculation, and the relatedness-based mating preference requires just a one-line `mateChoice()` callback. If we run this model five times with the `mateChoice()` callback, the average of the reported heterozygosity values across those runs is `0.00163`, whereas the average across five runs without the mate choice callback is `0.00426`. Clearly the `mateChoice()` callback is having a pronounced effect on the nucleotide heterozygosity observed in the model, as intended (with a two-sample independent *t*-test p-value of `0.0011`, if you're skeptical).

Incidentally, it would also be possible to implement the tendency towards mating with kin using a `modifyChild()` callback instead. That callback would evaluate the relatedness of the two parents of the proposed child, and would tell SLiM to short-circuit generation of the child, with some probability, if the relatedness of the parents was not sufficiently high. If only a weak inbreeding effect is desired, this might be much faster than the `mateChoice()` scheme shown above, since for the generation of a typical child only one or a few relatedness values would need to be calculated, and the relatively large overhead of running the `mateChoice()` callback would be avoided. This should be very simple, so it is left as an exercise for the reader.

13.3 Mortality-based fitness

Normally, SLiM uses fitness values as mating weights: high-fitness individuals are more likely to be chosen as mates than low-fitness individuals (see section 19.2.2). By default, SLiM does not model mortality; there is no concept of individuals dying before reaching reproductive age (except for the suppression of child generation with a `modifyChild()` callback, which can be viewed as a type of mortality-based fitness; see chapter 12). However, it is straightforward to add mortality to a model: if model mechanics dictate that an individual dies, then it can be given a fitness of zero, which means that it cannot possibly be chosen as a mate; effectively, it has been removed from the population (although it will remain as an individual in the population until the next generation starts; there is no way to actually remove dead individuals from the population).

(Note that this section is aimed primarily towards WF models; in nonWF models, as discussed in section 1.6, fitness translates into mortality anyway, rather than influencing mating, so every nonWF model is a model of mortality-based fitness. However, in nonWF models it can still be useful to explicitly kill off a specific individual by making its fitness zero; see, for example, the recipe in section 15.5.)

Here we will look at three different models of how mortality might be implemented. One model converts the fitness effects of mutations directly into mortality using a `fitness()` callback. This might be a good way to model death due to deleterious genetic factors. The second model is a `tag`-based model (see section 1.3 and sections cited therein); if individuals die, their `tag` value is set to zero, and then a special `fitness()` callback is used to reduce the fitness of tagged individuals to zero. This might be a good way to model death due to non-genetic factors, such as predation. The third model uses the `fitnessScaling` property of `Individual`, a new feature introduced in SLiM 3.0.

One question regarding mortality-based fitness might be: what difference does this make? Why would one wish to model mortality-based fitness rather than (or in addition to) mating-based fitness? The answer is that the two types of fitness have different effects on the distribution of the number of offspring generated by individuals. With mating-based fitness, all individuals of a given low fitness value are equal in the offspring-production game; the expected number of offspring is the same for all, and is lower than the expected number of offspring for a high-fitness individual.

With mortality-based fitness, however, all individuals of a given low fitness value are *not* equal, by the time mating season arrives: some are alive, and some are dead. Those that are alive have an expected number of offspring that is just as high as a high-fitness individual; they survived to mating season, and now the playing field is even. Those that are dead, on the other hand, have an expected number of offspring of zero. What the evolutionary consequences of this difference might be is not the focus here; but there clearly is a difference, and so we want to be able to model mortality-based fitness.

So, with no further ado, let's look at our first model:

```
initialize() {
    initializeMutationRate(1e-7);

    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "f", -0.005);    // deleterious
    m2.convertToSubstitution = F;

    initializeGenomicElementType("g1", c(m1,m2), c(1.0,0.1));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
}
fitness(m2)
{
    // convert fecundity-based selection to survival-based selection
    if (runif(1) < relFitness)
       return 1.0;
    else
       return 0.0;
}
10000 late() {
    sim.outputMutations(sim.mutationsOfType(m2));
}
```

Mutations are mostly neutral (`m1`) but occasionally slightly deleterious (`m2`), and the deleterious mutations are not converted to substitutions when they fix (using `m2.convertToSubstitution = F`), since they should continue to cause mortality. At the end of a run, the model uses `outputMutations()` to print information about all of the `m2` mutations existing in the population (include those that have fixed, since they do not get substituted).

The interesting part of the model is the `fitness()` callback. It converts a fitness effect for an `m2` mutation (which will be `0.995` if homozygous and `0.9975` if heterozygous, given the dominance coefficient of `0.5` used for `m2`) into either `0` or `1`, with the probability of a fitness of `1` being equal to the fitness effect of the focal mutation in the individual. If the new fitness value is `0`, the focal `m2` mutation has resulted in mortality; the individual will not mate, and is effectively dead. If the new fitness is `1`, on the other hand, the individual has survived the deleterious effects of the focal `m2` mutation, and that mutation will have no further deleterious effect; it will not influence the individual's expected number of offspring, since its fitness effect has been converted to `1`.

There are a couple of things to note here. First of all, the mortality effects of multiple `m2` mutations in a single individual will combine multiplicatively, just as their non-mortality-based fitness effects would combine multiplicatively in SLiM without the `fitness()` callback. This is because the `fitness()` callback will be called for each `m2` mutation, and the probabilities of mortality that these callbacks cause will combine multiplicatively (as independent probabilities generally do).

Second, the way that this `fitness()` callback works depends on the `m2` mutations being deleterious, not beneficial. This is because for a beneficial mutation, `relFitness` would be greater than `1`, and so the comparison with `runif(1)` would always be `T`. On a more conceptual level, you can't be more likely to survive than a survival probability of `1`. If you wish to model beneficial mutations with a mortality-based effect, you would need to provide some baseline probability of mortality in the model, such that an individual with no mutations would still have, say, a probability of `0.5` of dying before reaching reproductive age. The presence of beneficial mutations could then reduce this probability of dying, down to the limit of a probability of `0.0`.

Third, there is no obstacle to combining this sort of mortality-based fitness effect with the usual mating-based fitness effects of SLiM, using other mutation types. There is nothing magical about this model; the `fitness()` callback here is just another `fitness()` callback, albeit one that (somewhat unusually) models a stochastic fitness effect that varies from individual to individual.

Now let's look at the second recipe for mortality-based fitness, this one driven by tags:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
}
late() {
    // initially, everybody lives
    sim.subpopulations.individuals.tag = 1;

    // here be dragons
    sample(sim.subpopulations.individuals, 100).tag = 0;
}
fitness(NULL) {
    // individuals tagged for death die here
    if (individual.tag == 1)
       return 1.0;
    else
       return 0.0;
}
10000 late() { sim.outputFull(); }
```

This model involves only neutral mutations of type `m1`. It has a `fitness()` callback that evaluates phenotypic fitness (in this case, mortality). Because the mutation type identifier for the `fitness()` callback is `NULL`, this is a *global* `fitness()` callback (see section 22.2) that is called once per individual per generation, without reference to any focal mutation, allowing a fitness effect to be generated that depends upon the overall state of each individual. This technique was previously used in section 13.1, where it was used to define the fitness effect of individual phenotypes determined by additive QTLs.

In this case, the "overall state" that the `fitness(NULL)` callback models is mortality due to having previously been tagged as dead. The `fitness(NULL)` callback simply returns `1.0` (lived) for individuals with a `tag` of `1`, and `0.0` (dead) for all others. The `tag` values are assigned in a `late()` event that runs near the end of every generation. In this model, `100` individuals out of the `500` in the population are chosen for death at random using the `sample()` function, but that is just an arbitrary placeholder for whatever sort of mortality-generating logic you might wish to implement in your model – predation, social interactions, developmental disorders, or anything else. Indeed, the logic could depend on the genetics of individuals in some way, combining the approach of this recipe with that of the previous recipe.

One note here is that the tagging logic occurs in a `late()` event. That is because `tag` values for newly generated offspring need to be assigned before fitness values for the new offspring generation are calculated, and a `late()` event is the right time to do that (see the generation cycle diagram in chapter 19). This has the side effect that mortality does not occur in the first generation at all; `tag` values have not been assigned, and so the whole set of machinery that generates mortality is not yet active. This might sound unfortunate, but in fact it is the way the previous recipe worked as well, and indeed it is the way that models in SLiM generally work: since the first parental generation starts out with empty chromosomes, and since new mutations are added to genomes during offspring generation, the first generation generally is not subject to any selection unless a model explicitly adds mutations to the first generation and then forces a re-evaluation of the fitness of that generation using `SLiMSim`'s `recalculateFitness()` method. That would be an option here as well, if deemed necessary; code could be added to set up `tag` values in an `early()` event in generation `1`, and then a call to `recalculateFitness()` in an `early()` event in generation `1` could cause the `tag` values to produce mortality in the parentals. However, having a first generation of neutral dynamics is usually not a problem, since models usually want to start from a neutral equilibrium state anyway; in practice, a model would usually run neutrally for many generations as "burn-in", and then some mortality-generating mechanism of interest would "kick in". In that sort of scenario, this issue of whether or not mortality occurs in the first parental generation is irrelevant. Alternatively, another type of model would start off immediately with the mortality effect being active, but would run until equilibrium was reached; in that case, again, whether mortality occurs in the first parental generation is unlikely to be important, since the final equilibrium state will usually not depend upon that detail. Nevertheless, it can be forced to occur, as described above, if deemed necessary.

OK, with that discussion out of the way it is time for the third and final recipe for mortality-based fitness:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
}
late() {
    // here be dragons
    sample(sim.subpopulations.individuals, 100).fitnessScaling = 0;
}
10000 late() { sim.outputFull(); }
```

This is equivalent to the second recipe, but is much simpler and runs much faster. In this recipe, we use the `fitnessScaling` property of `Individual`, which was added in SLiM 3.0, to directly kill off individuals in the `late()` event, rather than using `tag` values and a `fitness(NULL)` callback that translates those tag values into fitness effects. The `fitnessScaling` values get multiplied into each individual's calculated fitness value, just as the value returned by the `fitness(NULL)` callback did in the second recipe. Note that it is not necessary to initialize the `fitnessScaling` values to `1.0` in each new generation; SLiM does that automatically.

The second recipe, then, is generally inferior, but is included for a couple of reasons. One is simply the historical reason that, prior to SLiM 3.0, it was the right way to implement mortality-based fitness, and might still be of interest for that reason alone. It also illustrates the use of tag values in a very simple model, which is perhaps useful. Finally, since it is strictly equivalent to the third recipe, it might expose the underlying logic of the third recipe more clearly; using the fitnessScaling property is a bit "magical", with a lot of what is happening hidden behind the scenes, whereas the second recipe shows the mechanism more explicitly.

Note that something along the lines of the first recipe could also be implemented using `fitnessScaling`, in fact, with a little bit of scripting. To achieve this, you would first make the selection coefficient of the `m2` mutations be `0.0`, rather than `-0.005`, so that they are neutral as far as SLiM's fitness-calculation machinery is concerned. Then, you would loop through the individuals in a `late()` event, and for each individual you would count the number of `m2` mutations, determine the survival probability based upon that count (`0.995^(count/2)`, perhaps), draw a random number to determine survival, and set `fitnessScaling` to `0` for the individuals that did not survive. This would not be quite the same as the first recipe, though, since it would not account for homozygosity versus heterozygosity (i.e., dominance effects) in the same way. Which strategy is preferable would depend upon the biology you were trying to model.

13.4 Reading initial simulation state from an MS file

At the beginning of execution of a SLiM model, the genomes of all individuals are empty; they contain no mutations. Mutations can be introduced explicitly in script (see section 10.1), or the saved state of a SLiM simulation can be read in to provide a non-empty initial state (see section 21.12.2, and section 10.2 for an example). Sometimes, however, information about the desired initial state of the model will be in a file that is in a non-SLiM format, and you will want to read that file in and create that initial state in the model. In this section, we will examine a recipe for reading in a file that is in the popular "MS" format. This can be useful, since MS uses a very fast coalescent method to generate genetic diversity in a neutral model; it can be used to generate an initial "burn-in" state that a SLiM model can then use as a starting state simulations.

As a first step, we need a file in MS format to read in. We could use MS to generate that, of course, but instead, for illustration purposes here, we will use a simple neutral SLiM model:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 1000);
}
20000 late() {
    p1.outputMSSample(2000, replace=F, filePath="~/Desktop/ms.txt");
}
```

Notice that the `outputMSSample()` call samples without replacement, using `replace=F`, and it requests `2000` samples – twice the size of the population, because there are two genomes per diploid individual. This means that the call will output not just a sample, but the full state of the entire population. The result of this model is a standard MS-format file, saved out to `ms.txt`:

```
//
segsites: 345
positions: 0.0047300 0.0048000 0.0053201 0.0063001 0.0068701 0.0072201
0.0078301 0.0098501 0.0140401 0.0144601 0.0162002 0.0196102 0.0236902...
00100000000010000000000000001000100100101100000000100001010000000000000000
00000000000000000001000000010011000100000000111000100000000000000000001100
10000001111000100000000000000001001000001001000000101100100000001000010001
00100000000000000000000000001000000000010000000000000000000000010000000000
0000000000000000100000000000000000000000000000100
01100000000000000000000000000000100001000001100001000010101000001000000010
00000000000010000000000000000000000000001010000000000000100010000000000001
00000100000000000000000000000000000010000000010000000100100000000000010000
00000000001100000000000000001000000000010000000000000000001000010000000000
0000000000000000100000000000000000000000000000000
...
```

Ellipses have been used here to abbreviate the lengthy content of the file. It begins with a `//` line that marks the beginning of a sample block. A `segsites:` line then gives the number of segregating sites per sample, and a `positions:` line gives the positions, in the interval [0,1], of each segregating site. The remainder is a series of samples, one per line, with `1` and `0` values indicating whether each corresponding mutation is (`1`) or is not (`0`) present in that genomes.

Now let's look at a recipe for reading this file back in and instantiating it into neutral mutations. Here we use the same chromosome length, population size, and other parameters, so that the loaded state corresponds to the model's defined dynamics. This is not required, but be careful that what you are doing makes sense. Here is the recipe:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 late() {
    sim.addSubpop("p1", 1000);

    // READ MS FORMAT INITIAL STATE
    lines = readFile("~/Desktop/ms.txt");
    index = 0;

    // skip lines until reaching the // line, then skip that line
    while (lines[index] != "//")
       index = index + 1;
    index = index + 1;

    if (index + 2 + p1.individualCount * 2 > size(lines))
       stop("File is too short; terminating.");

    // next line should be segsites:
    segsitesLine = lines[index];
    index = index + 1;
    parts = strsplit(segsitesLine);
    if (size(parts) != 2) stop("Malformed segsites.");
    if (parts[0] != "segsites:") stop("Missing segsites.");
    segsites = asInteger(parts[1]);
```

```
        // and next is positions:
        positionsLine = lines[index];
        index = index + 1;
        parts = strsplit(positionsLine);
        if (size(parts) != segsites + 1) stop("Malformed positions.");
        if (parts[0] != "positions:") stop("Missing positions.");
        positions = asFloat(parts[1:(size(parts)-1)]);

        // create all mutations in a genome in a dummy subpopulation
        sim.addSubpop("p2", 1);
        g = p2.genomes[0];
        L = sim.chromosome.lastPosition;
        intPositions = asInteger(round(positions * L));
        muts = g.addNewMutation(m1, 0.0, intPositions);

        // add the appropriate mutations to each genome
        for (g in p1.genomes)
        {
           f = asLogical(asInteger(strsplit(lines[index], "")));
           index = index + 1;
           g.addMutations(muts[f]);
        }

        // remove the dummy subpopulation
        p2.setSubpopulationSize(0);

        // (optional) set the generation to match the save point
        sim.generation = 20000;
    }
    30000 late() { sim.outputFull(); }
```

The action is in the generation 1 `late()` event, which first creates the `p1` subpopulation and then reads in the MS file and adds mutations to the individuals in `p1` as needed. It would be too tedious to explain this code line by line, so we will focus on just a few salient points.

First of all, the `readFile()` function is used to read in the MS data. This function returns a `string` vector, with one `string` element per line in the file. The rest of the code then processes these lines. First, a scan through the lines is conducted to find the `//` line that indicates the start of the actual sample data; MS files can have various information above that point that this code does not attempt to parse. Below that line should be a `segsites:` line and then a `positions:` line, as shown in the snippet above; the code scans for those lines and does some minimal error-checking.

Next, the recipe creates all of the mutations referenced by the MS data. This recipe assumes that these mutations are all neutral, since that is how MS would typically be used as input to a SLiM script. One twist here is that mutations cannot be created in isolation; according to SLiM's design, mutations must always reside in a `Genome` object. This recipe therefore creates a dummy subpopulation with a single individual, and throws all of the MS mutations into the first genome of that individual. This design may seem a bit odd, but it is harmless (nevertheless, it could be avoided if necessary, by adding the mutations in `p1` instead and then removing unreferenced mutations rather than adding referenced mutations).

Having created all of the mutations, the recipe then returns to processing input lines, which now are each a representation of one genome, as explained above. The `strsplit()` function is used to separate the `0` and `1` values into separate `string` elements, which are then converted to `integer` and then to `logical`. This results in a `logical` vector that indicates whether each corresponding mutation is or is not referenced by the focal genome. A call to `addMutations()` adds the selected mutations to the focal genome, and then the code moves to the next input line.

At the end, the dummy `p2` subpopulation is removed. Finally, the generation is set to `20000`, to dovetail with the fact that the simulation that generated the MS data ended at generation `20000`. This is optional, but can be helpful for keeping track of a multi-stage simulation of this sort.

This recipe is tailored to a somewhat specific situation – a neutral MS simulation to conduct a burn-in – but it should be adaptable to a wide variety of other situations. Indeed, a strategy very much like this could be used to read in empirical data regarding the genotypes of individuals in a natural population at various ecologically-relevant SNPs.

13.5 Modeling chromosomal inversions with a `recombination()` callback

In previous chapters we have seen four types of callbacks: `initialize()`, `fitness()`, `mateChoice()`, and `modifyChild()`. There is actually a fifth type of callback that is less commonly used: the `recombination()` callback (see section 22.5). This type of callback allows the script to modify the recombination breakpoints used by SLiM when generating a gamete to produce a new offspring individual. In most models, the standard user-defined recombination map set by `initializeRecombinationRate()` and perhaps `setRecombinationRate()` suffices, since usually all individuals in a simulation use the same recombination map (or perhaps different maps for males and females, which is supported by those calls as well). In some cases, however, recombination behavior needs to vary at the individual level. That would be true in a model of the evolution of recombination itself, for example; one would want individual-level variation in recombination behavior, presumably controlled by the genetics of individuals, to evolve in response to natural selection. It is also true in the model we will explore here: a model of the evolutionary effects of chromosomal inversions. We'll build this model step by step. Here's our starting point:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "f", -0.05);  // inversion marker
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-6);
}
1 {
    sim.addSubpop("p1", 500);
}
1 late() {
    // give half the population the inversion
    inverted = sample(p1.individuals, integerDiv(p1.individualCount, 2));
    inverted.genomes.addNewDrawnMutation(m2, 25000);
}
1:9999 late() {
    // assess the prevalence of the inversion
    pScr = "sum(applyValue.genomes.containsMarkerMutation(m2, 25000));";
    p = sapply(p1.individuals, pScr);
    p__ = sum(p == 0);
    pI_ = sum(p == 1);
    pII = sum(p == 2);
    cat("Generation " + format("%4d", sim.generation) + ": ");
    cat(format("%3d", p__) + " --   ");
    cat(format("%3d", pI_) + " I-   ");
    cat(format("%3d", pII) + " II\n");

    if (p__ == 0) stop("Inversion fixed!");
    if (pII == 0) stop("Inversion lost!");
}
```

This initial model is just a model of neutral drift with an introduced deleterious mutation. The generation 1 `late()` event makes half of the population homozygous for a "marker mutation", of type `m2`, that indicates the presence of an inversion; however, the machinery to implement the inversion behavior is not yet present. Indeed, in this version of the model the marker mutation is typically rapidly lost, since it is deleterious with a selection coefficient of `-0.05`; this selection coefficient makes the marker mutation easy to see in SLiMgui, because it gets colored red. Below, we will fix the marker mutation to not be deleterious while retaining this helpful coloration in SLiMgui.

The other `late()` event in the above model produces output. Every generation, it prints a summary of how many individuals do not have the inversion, how many are heterozygous for it, and how many are homozygous for it (assessed using the very useful `sapply()` function with a script, `pScr`, that checks for the marker mutation using the fast special-purpose `Genome` method `containsMarkerMutation()`). It also checks for the inversion having been fixed or lost, and prints a message and stops if either of those outcomes has occurred. If we run the model as it now stands, we will get output something like this:

```
Generation    1: 250 --     0 I-   250 II
Generation    2: 134 --   256 I-   110 II
Generation    3: 142 --   223 I-   135 II
...
Generation   82: 467 --    32 I-     1 II
Inversion lost!
```

Producing this output in every generation makes for a whole lot of output, and it slows down the simulation, too. Let's add a couple of lines to the top of the `late()` event to make it run only every 50th generation instead:

```
    if (sim.generation % 50 != 0)
      return;
```

As explained above, we don't want the marker mutation to actually be deleterious; the purpose of that selection coefficient is just so that SLiMgui colors the marker mutations red. Instead, in this model we want the inversion marker to be subject to balancing selection strong enough to keep it near intermediate frequency. This is a proxy for the inversion itself (or more realistically, an unmodeled mutation within the inversion) having some sort of phenotypic effect that is under balancing selection in the environment. So now let's add a `fitness()` callback to create that balancing selection (see section 9.4.1 for more discussion of modeling frequency-dependent selection):

```
fitness(m2) {
    // fitness of the inversion is frequency-dependent
    f = sim.mutationFrequencies(NULL, mut);
    return 1.0 - (f - 0.5) * 0.2;
}
```

Notice that now, since the `fitness()` callback redefines the fitness effect of the marker mutations in all cases, the default fitness value of `-0.05` is no longer actually used by SLiM – but SLiMgui still uses that value to color the mutations red in its chromosome view. This is a nice trick for giving special mutation types, such as marker mutations, particular colors in SLiMgui.

Running the model now produces output that indicates that the marker mutation is indeed under balancing selection and is not lost:

```
Generation   50: 140 --   266 I-    94 II
Generation  100: 123 --   255 I-   122 II
Generation  150:  90 --   235 I-   175 II
Generation  200: 176 --   237 I-    87 II
Generation  250: 148 --   250 I-   102 II
Generation  300: 205 --   229 I-    66 II
...
```

So far so good, but our marker mutation is still just an ordinary mutation under balancing selection; we still have no machinery to make it model a chromosomal inversion in particular. Now we add the core of this recipe – a `recombination()` callback that prevents recombination within the inversion between homologous chromosomes that are heterozygous for the inversion:

```
recombination() {
    if (genome1.containsMarkerMutation(m2, 25000) ==
        genome2.containsMarkerMutation(m2, 25000))
      return F;

    inInv = (breakpoints > 25000) & (breakpoints < 75000);
    if (sum(inInv) == 0)
      return F;

    breakpoints = breakpoints[!inInv];
    return T;
}
```

Let's walk through this in some detail. First, the callback determines whether the parent individual that is generating the focal gamete is heterozygous for the inversion. The inversion only affects recombination if the parent is heterozygous, so in other cases the callback returns `F` immediately, a flag value indicating that no change to the proposed breakpoints is needed.

Next, a `logical` vector, `inInv`, is constructed that has `T` for proposed breakpoints that are within the inversion region, `F` otherwise. The positions of proposed breakpoints are supplied to the callback by SLiM in the `breakpoints` variable; that variable can also be set by the callback to change the proposed breakpoints as we will see momentarily. The inversion region is defined by the code here to stretch from base position `25000` to `74999` inclusive. Recombination positions fall immediately to the left of the given base position; in other words, crossover occurs between the specified base and the *preceding* base. For this reason, the logic here considers a breakpoint exactly at position `25000` to be outside the inversion. If there are no proposed breakpoints inside the inversion region, the callback returns `F` immediately. Note that our marker mutations were created originally, with the `addNewDrawnMutation()` call, at position `25000`, the first position within the inversion region that we have just defined. Any position within the inversion region would work equally well, but positions outside of the inversion region would not work, since recombination could then separate the marker mutation from the contents of the inversion.

Finally, the callback removes all proposed breakpoints inside the inversion by subsetting `breakpoints` with the negation of `inInv`, and then it returns `T` to indicate that the proposed breakpoints were changed. This achieves the desired goal of suppressing all recombination within the inversion region for gametes generated by heterozygote parents.

Note this callback is written to be very efficient, since it is called for every gamete produced by every individual in every generation. Whenever possible, it returns `F` to indicate that no change to the proposed breakpoints is needed; this allows SLiM to skip a bunch of extra work. It could be made even faster by caching each individual's inversion count in the individual's `tag` value in an `early()` event. We will not explore that here, but it is worth keeping in mind that pre-cacheing the results of static computations outside of frequently-called callbacks can improve performance.

Note also that this callback handles only suppression of ordinary recombination breakpoints. If you enabled gene conversion in your model (see section 6.1.3), you may also wish to make inversions modify how gene conversion occurs. That is easy to do, but is not shown in this recipe; see section 22.5 for further information.

So now we have a working model of chromosomal inversions, but it would be nice to have some quantitative evidence that it is working properly. For that, let's add a final output event:

```
9999 late() {
    sim.outputFixedMutations();

    // Assess fixation inside vs. outside the inversion
    pos = sim.substitutions.position;
    cat(sum((pos >= 25000) & (pos < 75000)) + " inside inversion.\n");
    cat(sum((pos < 25000) | (pos >= 75000)) + " outside inversion.\n");
}
```

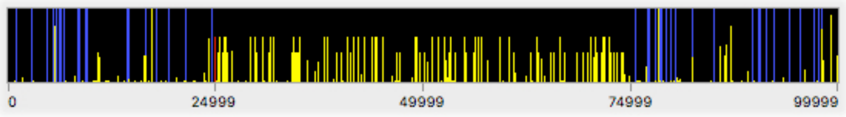
This event prints a list of the fixed mutations using `outputFixedMutations()`, as we've seen in other recipes. Then it looks at all of the mutations that have fixed during the simulation (kept by the `sim` object in its `substitutions` property), and extracts their positions. Finally, it tallies and prints the number of fixed mutations that occurred within the inversion region, versus the number that occurred outside. Without the inversion, these numbers would be expected to the roughly equal, since there are `50000` bases inside the inversion and `50000` outside, and indeed, if you comment out the recombination() callback and run the model, you will see something like this:

```
37 inside inversion.
40 outside inversion.
```

But with the recombination callback active, the results are very different:

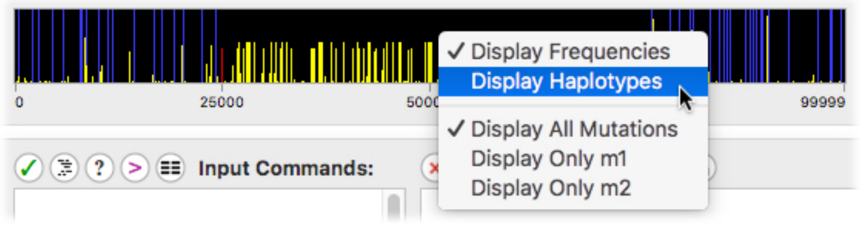
```
0 inside inversion.
43 outside inversion.
```

This can be seen graphically in SLiMgui. If display of fixed mutations is turned on with the F button to the right of the chromosome view, this is what things look like at the end of the run:

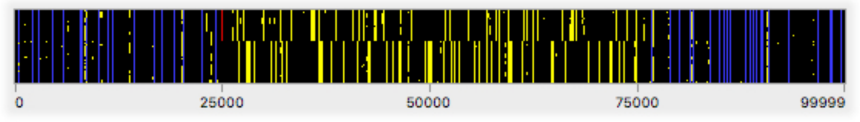


Many mutations outside the inversion have drifted to fixation. (To facilitate that happening quickly, this model uses a recombination rate of 1e-6, so that linkage disequilibrium with the inversion gets broken down quickly, but that is not an essential component of the model, just a way to get it to show interesting results more quickly.) Inside the inversion, however, there are two major haplotypes, and mutations within the inversion can't fix because they can't cross from one haplotype to the other. This is the result of suppression of recombination within the inversion; chromosomes containing the inversion accumulate one set of fixed mutations through drift, while chromosomes not containing the inversion accumulate a different set of fixed mutations.

While we're on the subject of haplotypes, this model is a particularly good testbed for looking at some advanced features of SLiMgui that facilitate the examination of haplotypes and linkage disequilibrium in SLiM. Let's run the model out to the end again, to reach a similar state to that shown above, and then control-click on the chromosome view to get a context menu that allows us to configure its display:

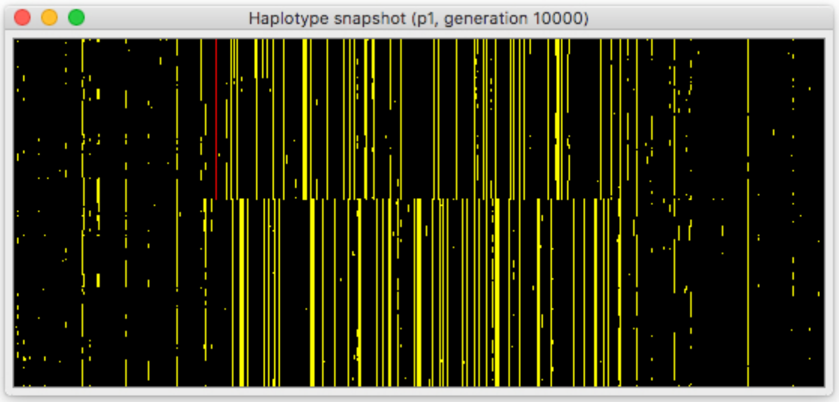


Select "Display Haplotypes" from the context menu, and the chromosome view changes to show the haplotypes that are in the population, clustered according to their genetic similarity:



Here the effect of the inversion is even clearer; outside of the inversion there are few mutations at high frequency and no apparent population structure, but inside the inversion the population has clearly differentiated into two completely different haplotypes with no admixture. The marker mutation indicating the inversion can be seen, associated with one of the two haplotypes.

This alternate display mode for the chromosome view is based upon just a small sample of the genomes from the selected subpopulation(s), allowing genetic clustering and display to be done in real time. It can also be useful to get a more comprehensive haplotype plot, based upon a larger sample or upon the entire population. To obtain that, choose Create Haplotype Plot from the Show Graph button's pop-up menu (or from the Simulation menu). This shows a panel that allows us to choose plot options; we can use the default options here, so click OK. After a progress panel (since the analysis can be quite lengthy with a large sample), a new plot window opens:



This shows essentially the same information as the chromosome view did above, but it is based upon all 1000 genomes in the population, and thus provides some additional detail. A context menu on the plot window, obtained with control-click or right-click, allows the appearance of the plot to be adjusted, and also allows the plot's image to be copied or saved as a file.

That completes this model of chromosomal inversions using a `recombination()` callback, but as usual there is much more that could be done. Rather than using balancing selection, for example, spatially varying selection among subpopulations could allow adaptive ecological divergence between subpopulations to arise as a result of the protection from recombination afforded by the inversion. It would also be interesting to model the rise of an inversion to high local frequency, in a model like that, to explore how inversions can facilitate divergence and speciation.

13.6 Modeling both X and Y Chromosomes with a Pseudo-Autosomal Region (PAR)

SLiM has built-in support for modeling either the X or Y chromosome when sex is enabled (see section 6.2.3). However, some models need to go beyond this built-in support. You might wish to model *both* the X and Y chromosomes, and you might even wish to model a pseudo-autosomal region (PAR) – a region in which recombination between the X and Y occurs freely, giving the region evolutionary dynamics similar to those of an autosome. Both males and females are diploid for genes in the PAR; females have two copies of the PAR on their two X chromosomes, whereas males have the same PAR on their X, and a homologous PAR on their Y. Because crossing over occurs freely between the X and Y within the PAR, genes in the PAR exhibit an autosomal pattern of inheritance rather than sex-linked inheritance.

Modeling this in SLiM is possible by implementing your own sex-chromosome mechanics, which is fairly straightforward. In this section we'll explore a simple model of neutral X and Y chromosome evolution with a single PAR connecting them. This model was provided by Melissa Jane Hubisz, and has been adapted for publication as a recipe here.

The basic model is quite simple:

```
initialize()
{
    initializeMutationRate(1.5e-8);
    initializeMutationType("m1", 0.5, "f", 0.0);     // PAR
    initializeMutationType("m2", 0.5, "f", 0.0);     // non-PAR
    initializeMutationType("m3", 1.0, "f", 0.0);     // Y marker

    // 6 Mb chromosome; the PAR is 2.7 Mb at the start
    initializeGenomicElementType("g1", m1, 1.0);     // PAR: m1 only
    initializeGenomicElementType("g2", m2, 1.0);     // non-PAR: m2 only
    initializeGenomicElement(g1, 0, 2699999);        // PAR
    initializeGenomicElement(g2, 2700000, 5999999);  // non-PAR

    // turn on sex and model as an autosome
    initializeSex("A");

    // no recombination in males outside PAR
    initializeRecombinationRate(c(1e-8, 0), c(2699999, 5999999), sex="M");
    initializeRecombinationRate(1e-8, sex="F");
}

// initialize the pop, with a Y marker for each male
1 late() {
    sim.addSubpop("p1", 1000);
    i = p1.individuals;
    males = (i.sex == "M");
    maleGenomes = i[males].genomes;
    yChromosomes = maleGenomes[rep(c(F,T), sum(males))];
    yChromosomes.addNewMutation(m3, 0.0, 5999999);
}

modifyChild() {
    numY = sum(child.genomes.containsMarkerMutation(m3, 5999999));

    // no individual should have more than one Y
    if (numY > 1)
      stop("### ERROR: got too many Ys");
```

```
		// females should have 0 Y's
		if (child.sex == "F" & numY > 0)
			return F;

		// males should have 1 Y
		if (child.sex == "M" & numY == 0)
			return F;

		return T;
	}

	10000 late() {
		p1.outputMSSample(10, replace=F, requestedSex="F");
	}
```

The `initialize()` callback sets up the genetic structure. This model turns on sex, because we want SLiM to track males and females for us, but it requests modeling of an autosome with `initializeSex("A")`; we will handle the tracking of the X versus Y chromosomes ourselves. To do that, we set up a special "marker" mutation type, `m3`, that will be used to tag Y chromosomes, as we will see shortly. We set up a 6 Mb chromosome with a 2.7 Mb PAR at the beginning; the PAR uses mutation type `m1` (through genomic element type `g1`), while the rest of the chromosome uses mutation type `m2` (through genomic element type `g2`), so that we can easily tell sex-linked mutations from pseudo-autosomal mutations later on. The only wrinkle during initialization is that we set up a recombination map in males that prevents recombination outside the PAR; females, which have two X chromosomes, are allowed to recombine freely.

Next we have a generation `1 late()` event that sets up the initial population. After making a new subpopulation in the usual way with `addSubpop()`, it gets the male individuals, selects only their second `Genome` objects, and adds an `m3` mutation to them to mark them as Y chromosomes. These marker mutations will be handled in the usual way by SLiM, so they will be inherited and will continue to mark Y chromosomes in future generations. Because recombination is prevented in males outside the PAR, they will stay associated with the non-PAR Y chromosome genetic information.

There is one problem with this scheme, however. When SLiM generates offspring, it has its own ideas about whether a given child ought to be male or female. We need to follow SLiM's guidance on this, otherwise our model will end up with individuals that SLiM considers female but that possess a Y chromosome, and individuals SLiM thinks are male but that have no Y. This is the purpose of the `modifyChild()` callback. It simply compares what SLiM expects for the sex of the child (`child.sex`) with the genetics that SLiM is proposing that the child will inherit (`child.genomes`). If they don't match, then it returns F to indicate that SLiM needs to choose new parents and try again. Note the `containsMarkerMutation()` method; this just checks for a mutation of a given type at a given position, which can be done quite quickly by SLiM. It is thus optimal when the position of a mutation (if it exists) is already known, as it is here.

Because `modifyChild()` callbacks get called quite frequently (once for each new offspring generated by SLiM, or even more in this case since the callback rejects some proposed children), the speed of callback code is essential. The callback above has very clear logic, but it is slow in several ways. It does a safety check that is never, in fact, hit (since the model works properly); it assigns a value into a variable, `numY`, which is relatively slow because it requires Eidos to set up a symbol table entry; it performs some unnecessary logical operations and tests (if `child.sex` is not `"F"` then it *must* be `"M"`, for example), and worst of all, it always calls `containsMarkerMutation()` for both child genomes even though in many cases the answer returned by one genome will already allow the callback to choose its action. With an optimized version of the callback, the model runs about 25% faster, a not-insignificant difference. The optimized callback:

```
modifyChild() {
    // females should not have a Y, males should have a Y
    if (child.sex == "F")
    {
      if (childGenome1.containsMarkerMutation(m3, 5999999))
        return F;
      if (childGenome2.containsMarkerMutation(m3, 5999999))
        return F;
      return T;
    }
    else
    {
      if (childGenome1.containsMarkerMutation(m3, 5999999))
        return T;
      if (childGenome2.containsMarkerMutation(m3, 5999999))
        return T;
      return F;
    }
}
```

If you examine this carefully, you should find that it will produce the same result in all cases (unless the model has already broken, such as by an individual having two Y chromosomes).

Finally, we have a `late()` event that outputs an MS-format sample from the females in the population; among other things, this establishes the end of the model as generation `10000`.

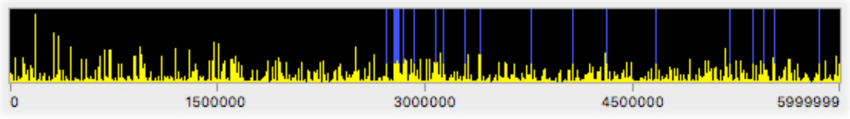
There is one remaining issue. Addressing it is optional, in a sense, but if we don't address it the model will run slower and slower until it grinds nearly to a halt. The problem is that while PAR mutations will fix and be converted into `Substitution` objects automatically by SLiM as usual, non-PAR mutations will not. This is because their threshold for fixation is lower than SLiM realizes; only a quarter of Genome objects are Y chromosomes, and only three-quarters are X chromosomes, so sex-linked mutations need to fix when they reach those frequencies, not a frequency of `1.0` as SLiM expects. Fixing this is not difficult, but it does require a bit of code:

```
1:10000 late() {
    // periodically remove m2 (non-PAR) mutations that are fixed in X or Y
    // m1 (PAR) mutations will be automatically removed when fixed
    if (sim.generation % 1000 == 0) {
      numY = sum(p1.individuals.sex == "M");
      numX = 2 * size(p1.individuals) - numY;

      // look at the mutations in a single Y chromosome
      // to find mutations that are fixed in all Y's
      firstMale = p1.individuals[p1.individuals.sex == "M"][0];
      fMG = firstMale.genomes;

      if (fMG[0].containsMarkerMutation(m3, 5999999)) {
        firstY = fMG[0];
        firstX = fMG[1];
      } else if (fMG[1].containsMarkerMutation(m3, 5999999)) {
        firstY = fMG[1];
        firstX = fMG[0];
      } else
        stop("### ERROR: no Ys in first male");
```

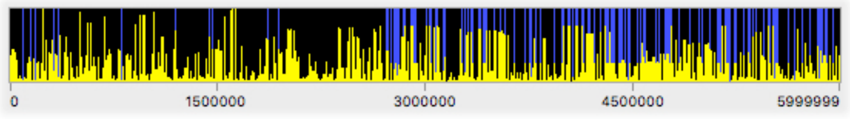
```
            ymuts = firstY.mutationsOfType(m2);
            ycounts = sim.mutationCounts(NULL, ymuts);
            removeY = ymuts[ycounts == numY];

            // now do the same for the X
            xmuts = firstX.mutationsOfType(m2);
            xcounts = sim.mutationCounts(NULL, xmuts);
            removeX = xmuts[xcounts == numX];

            cat("Gen. " + sim.generation + ": Removing ");
            cat(removeX.size() + "/" + removeY.size() + " on X/Y\n");

            removes = c(removeY, removeX);
            sim.subpopulations.genomes.removeMutations(removes, T);
        }
    }
```

This event should ideally be inserted before the generation `10000 late()` event that produces final output. It runs every `1000` generations, since the operation it performs is somewhat time-consuming; doing it every generation would be wasteful. It finds a male individual, and uses that individual as a template for finding and removing fixed sex-linked mutations. Any mutation that has fixed must be possessed by the template male (by the definition of "fixation"), so the code just gets all the mutations of type `m2` (non-PAR mutations) from the male's X and Y and checks them all for fixation. The fixation check itself is done using `mutationCounts()`, which returns the number of occurrences of the mutations – population-wide, in this case, because of the `NULL` passed for the first parameter. The event prints the number of X-linked and Y-linked mutations that it intends to remove, and then it removes them with `removeMutations()`. The optional `T` value passed for the second argument to `removeMutations()` (which is named `substitute`) indicates that SLiM should create `Substitution` objects for the removed mutations; we are notifying SLiM that those mutations are in fact fixed, even though SLiM doesn't realize it. If you don't care about that record-keeping, you can omit that optional `T` value, and the mutations will simply be removed.

And that's it. We've implemented tracking of Y chromosomes with marker mutations, we've guaranteed that those markers stay correctly synchronized with offspring sex, and we've added machinery to detect fixed sex-linked mutations and turn them into Substitutions just as SLiM does for autosomal mutations. If we run this model in SLiMgui with display of fixed mutations turned on (the F button to the right of the chromosome view), the behavior of the PAR versus the non-PAR regions is easy to see as soon as the first pass of the fixation check has run in generation `1000`:



The PAR, on the left, behaves as an autosome, so it takes a while for mutations to fix; one is close to fixation, but none has made it there yet. The non-PAR region, on the right, behaves as separate sex chromosomes that cannot recombine, and each sex chromosome is present in fewer copies than the PAR; mutations in that region thus have a smaller effective population size, and fix more rapidly. The Y, present in only a quarter as many copies as the PAR, fixes particularly quickly; all 20 of the fixations here are in fact on the Y. After generation `3000`, the situation is similar:



There have now been 19 fixations on the X, 120 on the Y, and only 11 in the PAR. The trend is clear, and it appears that our model of a pseudo-autosomal region is functioning as expected.

13.7 Forcing a specific pedigree through arranged matings

As we've seen in previous recipes, SLiM allows mating probabilities to be adjusted with `mateChoice()` callbacks, and sometimes `modifyChild()` callbacks can also be useful for implementing specific mating patterns since they can reject proposed offspring on the basis of information about the parents (as in, for example, the gametophytic self-incompatibility system implemented in section 11.3). Sometimes, however, it is desirable to go a step further, and simply dictate exactly what matings will occur in a given generation, in order to obtain a specific pedigree structure. This can also be implemented in SLiM, through a combination of tagging individuals and using a `mateChoice()` callback to allow only matings between individuals with specific `tag` values. In this section, we will look at a recipe that implements a very simple example of this: a founding event that begins with two mating events, involving disjoint sets of parents, to produce a founding population of two offspring (one from each mating). Note that this recipe is quite clunky and scales poorly, because the WF modeling framework is ill-suited to this task; see section 15.12 for a much more graceful and scaleable nonWF recipe for forcing a specific pedigree.

To begin with, here's a model that does what we want except for the forced pedigree:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
1000 late() { p1.setSubpopulationSize(2); }
1002: early()
{
    newSize = (sim.generation - 1001) * 10;
    p1.setSubpopulationSize(newSize);
}

1010 late() { p1.outputSample(10); }
```

This sets up an initial population of size `500`, lets it evolve to generation `1000`, and then triggers a bottleneck down to a population size of `2` (set in a `late()` event in generation `1000`, but actually taking effect for the offspring generation that is generated in `1001`). In effect, then, the original subpopulation is discarded, and we model the new founder subpopulation thereafter; modeling both could be done by adding the founder population as a new subpopulation, of course (see section 5.2.1). In generation `1002` and onward, the population grows linearly (for exponential growth, see section 5.1.2). The model terminates at the end of generation `1010` with the output of a subsample of the population. So far, so good; we've seen this sort of model many times.

The problem here is that with a severe bottleneck such as this, two undesirable things could happen. One, the same parent(s) could be chosen for both of the two founding offspring individuals, making the bottleneck more severe than we want. And two, because this is a hermaphroditic model (in which SLiM allows selfing by chance, if the same parent happens to be chosen twice), one or both of the founding offspring could be generated through selfing rather than biparental mating, again making the bottleneck more severe than intended. There are various ways to handle these issues (selfing in hermaphroditic models can be blocked with a simple `mateChoice()` callback, for example; see section 12.4).

For our purposes here, however, let's handle them by forcing SLiM to follow a specific pedigree for the founding event. We will choose four parents, A, B, C, and D, from the population, and we will force SLiM to mate A with B and C with D, each mating producing exactly one offspring. We'll do that by first modifying the `1000 late()` event that triggers the bottleneck:

```
1000 late() {
    p1.setSubpopulationSize(2);
    p1.individuals.tag = 0;
    parents = sample(p1.individuals, 4);
    parents[0].tag = 1;
    parents[1].tag = 2;
    parents[2].tag = 3;
    parents[3].tag = 4;
}
```

This event now not only triggers the founding bottleneck, but also chooses four parents from the original subpopulation using `sample()` – which by defaults samples without replacement, as desired – and marking them with unique `tag` values. The `tag` values of all other individuals are set to `0`. We can now identify A, B, C, and D using the `tag` values `1:4`. Next we need to force matings only between A and B, and C and D. We'll do that with a `modifyChild()` callback:

```
1001 modifyChild()
{
    t1 = parent1.tag;
    t2 = parent2.tag;

    if (((t1 == 1) & (t2 == 2)) | ((t1 == 2) & (t2 == 1)) |
       ((t1 == 3) & (t2 == 4)) | ((t1 == 4) & (t2 == 3)))
    {
       cat("Accepting tags " + t1 + " & " + t2 + "\n");
       parent1.tag = 0;
       parent2.tag = 0;
       return T;
    }

    cat("Rejecting tags " + t1 + " & " + t2 + "\n");
    return F;
}
```

This callback gets the `tag` values of the two parents of each proposed child. If the parents are A and B (which could be tags `1` and `2`, or tags `2` and `1`), the child is accepted; similarly if the parents are C and D. In that case, the `tag` values of the parents are set to `0` to ensure that those parents will not be allowed to mate a second time. If the parents don't pass the test, the callback simply rejects the proposed child by returning `F`, causing SLiM to try a new pair of parents.

This works well, except that there will be a noticeable pause at generation `1001`. Looking at the diagnostic output produced by the model shows why; there are a great many lines stating "`Rejecting tags 0 & 0`", quite a few lines stating things like "`Rejecting tags 2 & 0`", and exactly two lines stating something like "`Accepting tags 4 & 3`" and "`Accepting tags 1 & 3`". In other words, the model is having to reject a very large number of proposed children in order to achieve the desired pedigree. If the initial subpopulation were, say, `50000` individuals instead of `500`, this small problem would become a huge problem, as the model ground to a halt for perhaps days or weeks searching for acceptable mating pairs. Happily, there is a way to optimize the model to eliminate the problem, by adding a `fitness()` callback:

```
1000 fitness(m1)
{
    if (individual.tag == 0)
       return 0.0;
    else
       return relFitness;
}
```

This callback simply removes all individuals with a `tag` value of `0` from the mating pool, by declaring their fitness to be `0.0`. Although it removes all unchosen parents from the mating pool, it does not suffice in itself; without the `modifyChild()` callback as well, this `fitness()` callback would still allow A to mate with C, D to self, etc. But in conjunction with the `modifyChild()` callback, it reduces the mating pool to just the focal individuals we want, and thus greatly speeds up the process of filling the desired pedigree.

Note that this callback is defined for generation `1000`; we want to manipulate the fitness values of the individuals that will be parents in generation `1001` (the founding event generation), and those individuals are the offspring generated in generation `1000`, and thus have their fitness values calculated at the end of generation `1000`. When you're juggling individuals with different callbacks like this, you need to consult the generation life cycle (see chapter 19) very carefully!

With this callback in place, it takes only a few tries to get the matings we want, as for example:

```
Rejecting tags 2 & 4
Rejecting tags 1 & 1
Accepting tags 1 & 2
Rejecting tags 0 & 4
Rejecting tags 0 & 3
Accepting tags 4 & 3
```

The appearance of `tag` value `0` here is because parents `1` and `2` were accepted and produced an offspring, and thus their `tag` values were set to `0`. This did not remove them from SLiM's mating pool, since their fitness values were not recalculated; it merely marks them so that the `modifyChild()` callback can avoid using them again. Of course these diagnostic messages are just for illustration purposes anyway, and would be removed from a production model.

Note that the scheme here using `sample()` chooses parents for the founding population with equal weights. This is a neutral model, so that is fine, but even in a non-neutral model this might be desirable, depending upon the nature of the founding event; a storm that blows a handful of birds off-course to an isolated island, for example, might select the founding individuals completely at random, without regard for the fitness they would have had in their original habitat, and so the simple call to `sample()` shown here would be appropriate. But of course any other method of choosing the founders may be used. To sample parents weighted by their fitness values, as SLiM normally does when choosing parents, one could just obtain the fitness values for all parents, with a call to `cachedFitness(NULL)` on the parental subpopulation, and pass that vector directly to `sample()` as the weights to be used in sampling.

This is almost the simplest possible pedigree we could force, but the recipe can be generalized easily. For example, we could force more than one offspring to be generated by a given pair of parents if we wished, either by using more `tag` values to represent different states (when A and B are about to generate their first child, change their `tag` values to `5` and `6`, and allow parental pair `5`/`6` to also generate an offspring, for example), or by adding a counter to the parental individuals using the `setValue()` / `getValue()` facility of the `Individual` class (see section 21.6.2) to track how many children they have generated already; their `tag` values would not be reset to `0`, removing them from the parent pool, until that counter reached the desired value.

Similarly, this recipe could be extended to a larger pedigree, involving more parents and more offspring, simply by using more `tag` values. However, if you wanted to implement a large, complex pedigree involving many matings the implementation might get rather lengthy and cumbersome, with manual setting and checking of a large number of different `tag` values.

This recipe could also be extended to work over multiple generations, just by doing the same thing over again: `tag` the chosen parents, reject offspring that aren't from parents with the desired `tag` values. It would be straightforward, if admittedly a bit clunky, to reproduce an entire multigenerational pedigree of, say, a given royal family with a high rate of inbreeding and a deleterious trait such as hemophilia. To do this, first assign a unique number to each individual on the pedigree chart you want to model; then use those numbers as the `tag` values for the individuals in the model. If C is the child of A and B, the `modifyChild()` call back would, when deciding to allow A and B to mate to produce C, also set the `tag` value for the proposed offspring to mark that individual as C. Implemented across the board, this would allow the identity of every specific individual throughout the multigenerational pedigree to be tracked with precision.

As mentioned above, section 15.12 has a much more scalable recipe for forcing a specified pedigree using a nonWF model; that recipe is recommended for most users over this recipe.

13.8 Estimating model parameters with ABC

One major use of simulation models is to try to better understand an empirical system by comparing simulated results with empirical data. For example, one might have an observation from an empirical system, and have a guess as to a model that approximates that empirical system well; one might then want to know the value of a particular parameter of that model that produces the best possible fit of the model to the data. In this recipe we'll explore doing this using a technique called Approximate Bayesian Computation (ABC). This is quite a complex topic, and we will not attempt to provide a thorough introduction to it here; please use the internet to inform yourself further regarding the assumptions, limitations, and caveats involved in this method, as well as about the underlying theoretical framework upon which it rests.

In this recipe we're going to branch out a bit and present `R` code as well as Eidos code. The `R` code will run the ABC process, while the Eidos code will run the SLiM simulation that provides the ABC process with the information it needs. Let's start with the Eidos code:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 999999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 100); }
1000 late() { cat(sim.mutations.size() + "\n"); }
```

This is a trivial model, obviously. We start with a population of size `100`, and model neutral mutations in that population. The model is allowed to equilibrate until generation `1000`, at which point the number of segregating mutations detected in the population is printed. Simple and fast, which is important since ABC is going to run it a whole bunch of times.

To tie this back to an empirical question, this model would be a reasonable starting place if you said: "I have a population of size 100 that I have sampled comprehensively, and the analysis I've done tells me there are 262 segregating mutations in the population. I think the population has been about size 100 for a long time, so it's at equilibrium (to the extent that a small population evolving under drift is ever at equilibrium). I know the recombination rate and the chromosome length, but not the mutation rate. What's my best guess, and what's the posterior distribution around that guess?" So now we've got a SLiM model of that scenario, with a guess of `1e-7` hard-coded into it. Let's tweak the model by replacing the mutation rate with a symbolic constant:

```
        initializeMutationRate(mu);
```

We could define the constant `mu` at initialization time with a call to the Eidos function `defineConstant()`, like:

```
        defineConstant("mu", 1e-7);
```

But let's not do that; instead, we will pass a value for it in to the simulation on the command line. To do this, let's first save the model to a file called "abc.slim" in our home directory (we will assume that the file is then at the path `~/abc.slim`, as it is on most Unix systems including Mac OS X). If we run this model at the command line, we get an error about the undefined constant:

```
    darwin:~ bhaller $ slim ~/abc.slim
    ...
    ERROR (EidosSymbolTable::_GetValue): undefined identifier mu.

    Error on script line 2, character 24:

       initializeMutationRate(mu);
                              ^^
```

But we can pass a value for the constant in, using the `-d` (`-define`) command-line option (see section 17.2):

```
    darwin:~ bhaller $ slim -d mu=1e-7 ~/abc.slim
    ...
    262
```

This defines `mu` to be `1e-7` at the very beginning of the model, before the first `initialize()` callback is called. This run of SLiM is actually where the value of `262` came from, above; it's the value from our "empirical system" (i.e., this first run of our model), for which we're going to try to recover an estimate of `mu` using ABC. In practice, such observed values would probably come from actual empirical data.

So now we have a working model at `~/abc.slim` that expects a value for a constant `mu` to be supplied to it on the command line, and the last line of the output it generates is the outcome of the model – the number of segregating mutations observed in the population at equilibrium. The next step is to write some R code to run our model, given a random number seed and `mu`:

```
    runSLiM <- function(x)
    {
        seed <- x[1]
        mu <- x[2]
        #cat("Running SLiM with seed ", seed, ", mu = ", mu, "\n");
        output <- system2("/usr/local/bin/slim", c("-d", paste0("mu=", mu),
           "-s", seed, " ~/abc.slim"), stdout=T)
        as.numeric(output[length(output)])
    }
```

The `system2()` function of `R` is used to run SLiM with the desired command-line arguments, and the output is collected as a `character` vector of output lines. Note that this function takes the seed and `mu` values as a single vector, `x`; this is because of the design of the `R` package we will use to run the ABC in a moment. First, let's test this function:

```
> runSLiM(c(100030, 1e-7))
[1] 281
```

We get a different result than before, since a different random number seed was used, but it seems to work fine. So now we have R running our SLiM model for us; the next step is to actually run an ABC analysis. For this, we will use the package EasyABC, available through CRAN:

```
library(EasyABC)

# Set up and run our ABC
prior <- list(c("unif", 1e-9, 1e-6))
observed <- 262

ABC_SLiM <- ABC_sequential(method="Lenormand", use_seed=TRUE,
    model=runSLiM, prior=prior, summary_stat_target=observed,
    nb_simul=1000)
```

The EasyABC package has many different options for running ABC analyses, including several "sequential" ABC methods that try to arrive at an answer more quickly through successive rounds of ABC, and several ways of running the ABC inside an MCMC (Markov Chain Monte Carlo) process, a particularly powerful way of converging rapidly on the posterior distribution of the ABC. We have chosen the "Lenormand" method, since it is simple to set up, is happy to run with only one unknown parameter (which some of the other methods don't seem to be), and converges fairly quickly. Since ABC is a Bayesian method, we also need a prior for mu; we have chosen a uniform prior from 1e-9 to 1e-6, since that encompasses the range of mutation rates we think would be likely in our empirical system, and since we have no information about which values within this range are more or less likely. We also need to tell EasyABC how many runs we want to perform; the nb_simul parameter does that (sort of – see the documentation), and the value of 1000 here should give us quite a good posterior distribution at the expense of longer runtime (a value of 100 actually works pretty well already).

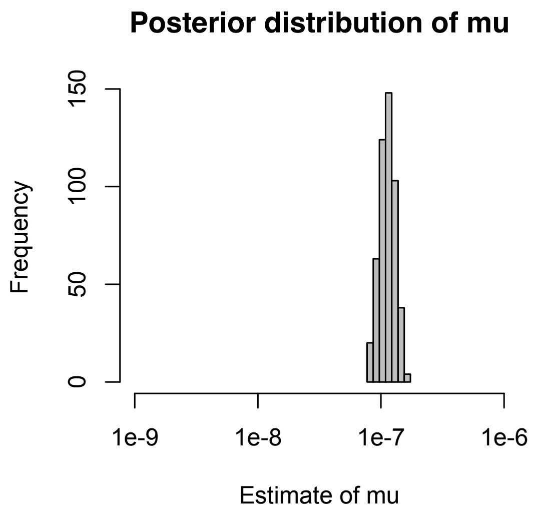
The final line, which actually runs the ABC analysis, will probably take several minutes, depending upon the speed of your machine. When it finishes, ABC_SLiM contains information about the ABC run. Details about that information can be found in EasyABC's documentation; we will not explain it here, but we will use it to extract the results we want. First of all, to get the best fit estimate from a one-parameter ABC like this, one typically wants the sum of the weighted average of the values chosen by the ABC:

```
> sum(ABC_SLiM$param * ABC_SLiM$weights)
[1] 0.0000001134854
```

The ABC did quite a good job of recovering the actual value of mu, 1e-7, that was used to generate the target value of 262. We can also plot the posterior distribution for mu that was arrived at by the ABC analysis, using this R code:

```
log_param <- log(ABC_SLiM$param, 10)
breaks <- seq(from=min(log_param), to=max(log_param), length.out=8)

quartz(width=4, height=4)
hist(log_param, xlim=c(-9, -6), breaks=breaks, col="gray",
    main="Posterior distribution of mu", xlab="Estimate of mu", xaxt="n")
axis(side=1, at=-6:-9, labels=c("1e-6", "1e-7", "1e-8", "1e-9"))
```

This code converts the posterior distribution data to a log scale manually and plots it on that scale, for clarity; there are probably better ways to do that. The quartz() call just opens a graphics device on Mac OS X; if you're on a different platform you will probably have to change that to your platform-specific graphics device call. Apart from those details, the code is pretty standard. The resulting plot looks like this:



We started with a uniform prior from `1e-9` through to `1e-6`, providing the ABC analysis with no information as to which values within that range were more likely. By doing quite a few runs of SLiM (12500, as it happens), the ABC narrowed that range down considerably, effectively ruling out a large part of it completely, and it gave us a posterior distribution showing which values of `mu` would be most likely to produce the observed number of segregating mutations, `262`, that was observed empirically. All in just a few lines of Eidos and a few lines of `R`; not bad!

This completes our foray into Approximate Bayesian Computation in SLiM and `R`. This topic can be pursued much further: estimation of the joint distribution of multiple parameters, usage of a Markov Chain Monte Carlo (MCMC) method for running the ABC (which is also supported by the EasyABC package), delving into the often difficult problem of priors, and so forth. But this recipe should provide a starting point for such explorations.

13.9 Tracking true local ancestry along the chromosome

Ancestry, relatedness, pedigree, and similar concepts are often important in forward genetic simulations such as those run by SLiM. Depending upon exactly what you need, there are several different approaches to these sorts of questions in SLiM:

- The `subpopID` property of mutations (section 21.8.1) keeps track of the subpopulation in which a given mutation originated. In an admixture model in which you want to determine whether a given mutation originally arose in one subpopulation or another, this is often all you need. Note also that if you are adding mutations yourself using `addNewMutation()` or `addNewDrawnMutation()`, you can set the `subpopID` in those calls to whatever value you wish. The `subpopID` property is writeable, so you can also change it later to any `integer` value (including some type of ancestry information).
- Mutation types can also be useful for tracking ancestry information. If different mutation types are used for mutations with different origins in your model, they can then be used to determine the origin of each mutation later, and SLiM's methods for retrieving and counting the mutations of a given mutation type can be used to separate out mutations of different origins. This approach will work even in non-admixture models in which all

mutations originate in a single subpopulation, as long as you can classify mutations according to their ancestry at the point when they originate (in a `modifyChild()` callback that looks at the parents to determine an ancestry group, for example). The mutation type of mutations can be changed with the `setMutationType()` method.

- By enabling an optional feature, SLiM can do pedigree-based tracking of the ancestry of individuals for the purposes of calculating relatedness, finding "trios" of parents and an associated offspring, and so forth (see section 13.2). This provides information about relatedness and ancestry at the level of individuals, rather than the level of mutations. Pedigree-based arranged matings can also be implemented (see section 13.7).
- If tree-sequence recording is turned on (see section 1.7 and chapter 16), it provides a type of true local ancestry tracking for every position along the chromosome. This is similar in some ways to this recipe, but much more efficient, and was added in SLiM 3.

Sometimes it is desirable to track relatedness not at the individual level with a pedigree, or at a mutational level with `subpopID` or mutation types, but instead at the level of chromosomal regions – perhaps down to the ancestry of each individual base position along the chromosome. In this way, the ways that assortment, recombination, selection, and drift determine the ancestry at each position can be analyzed. This type of relatedness tracking is also possible in SLiM, even when not using tree-sequence recording; we will explore an example in this section.

Models can implement "true local ancestry" tracking themselves using marker mutations – mutations which have no selective effect, and are not meant to represent actual mutational changes to genomes, but instead simply mark particular positions on particular genomes for future reference. The recipe in section 13.5 used a marker mutation to track individuals possessing a chromosomal inversion, for example, and in 13.6 a marker mutation was used to mark Y chromosomes in a model of a pseudo-autosomal region shared between sex chromosomes. Here marker mutations will be used at every position, to indicate ancestry. At the end, the model will assess the average ancestry, across the subpopulation, at every chromosome position.

Here is the complete recipe:

```
initialize() {
    defineConstant("L", 1e4);                     // chromosome length

    initializeMutationRate(0);
    initializeMutationType("m1", 0.5, "f", 0.1);   // beneficial
    initializeMutationType("m2", 0.5, "f", 0.0);   // p1 marker
    m2.convertToSubstitution = F;
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, L-1);
    initializeRecombinationRate(1e-7);
}

1 {
    sim.addSubpop("p1", 500);
    sim.addSubpop("p2", 500);
}

1 late() {
    // p1 and p2 are each fixed for one beneficial mutation
    p1.genomes.addNewDrawnMutation(m1, asInteger(L * 0.2));
    p2.genomes.addNewDrawnMutation(m1, asInteger(L * 0.8));

    // p1 has marker mutations at every position, to track ancestry
    p1.genomes.addNewMutation(m2, 0.0, 0:(L-1));
```

```
        // make p3 be an admixture of p1 and p2 in the next generation
        sim.addSubpop("p3", 1000);
        p3.setMigrationRates(c(p1, p2), c(0.5, 0.5));
    }

    2 late() {
        // get rid of p1 and p2
        p3.setMigrationRates(c(p1, p2), c(0.0, 0.0));
        p1.setSubpopulationSize(0);
        p2.setSubpopulationSize(0);
    }

    2: late() {
        if (sim.mutationsOfType(m1).size() == 0)
        {
          p3g = p3.genomes;

          p1Total = sum(p3g.countOfMutationsOfType(m2));
          maxTotal = p3g.size() * (L-1);
          p1TotalFraction = p1Total / maxTotal;
          catn("Fraction with p1 ancestry: " + p1TotalFraction);

          p1Counts = integer(L);
          for (g in p3g)
            p1Counts = p1Counts +
              integer(L, 0, 1, g.positionsOfMutationsOfType(m2));
          maxCount = p3g.size();
          p1Fractions = p1Counts / maxCount;
          catn("Fraction with p1 ancestry, by position:");
          catn(format("%.3f", p1Fractions));

          sim.simulationFinished();
        }
    }

    100000 late() {
        stop("Did not reach fixation of beneficial alleles.");
    }
```

The broad outline here is straightforward. We model two subpopulations, `p1` and `p2`, which are created in the generation `1` event and configured in the generation `1` `late()` event. That `late()` event also sets up a new subpopulation, `p3`, that will be produced by admixing migrants from `p1` and `p2` in generation `2`. At the end of generation `2`, `p1` and `p2` are removed, and `p3` is allowed to evolve thenceforth until the termination of the model. This model is therefore a very simple model of the admixture of two subpopulations; more complex population dynamics could easily be used with the same ancestry-tracking mechanism shown here.

When `p1` and `p2` were configured, they were each set up to contain a beneficial mutation of type `m1`, fixed within the respective subpopulation. The new `p3` subpopulation therefore contains some genomes that originated in `p1` and contain that subpopulation's beneficial mutation (located at `L * 0.2` on the chromosome), and some genomes that originated in `p2` and contain that subpopulation's beneficial mutation (located at `L * 0.8` on the chromosome). The expectation is that recombination between those points will eventually produce at least one new genome that contains both beneficial mutations, and that subsequently both beneficial mutations will sweep to fixation in `p3`. The question we wish to investigate is the precise pattern of true local ancestry along the chromosome at the point when fixation of both beneficial mutations has just occurred.

To do this, the model adds a marker mutation of type `m2` at every position along every genome in `p1`, in the `1 late()` event. This is done using a single vectorized call to `addNewMutation()`, for greater efficiency; adding the mutations one by one would take a very long time, especially with a longer chromosome. These added markers indicate that a given chromosome position traces its ancestry to `p1`. In models with more complex demography involving more than two "parental" subpopulations, additional mutation types could be employed to indicate derivation from each of the possible ancestral subpopulations. An important point to understand is that because mutations in SLiM "stack" by default, these marker mutations have no effect whatsoever on the other mutations that might occur during a simulation; they are simply carried along, almost as if they were epigenetic marks of some sort on the genomes being simulated. For simplicity, this model does not include neutral mutations along the chromosome, and indeed it uses a mutation rate of `0`; but the ancestry-tracking mechanism shown here is compatible with any other model dynamics.

Thus configured, the model runs until both beneficial mutations either fix or are lost. This termination condition is checked in the `2: late()` event. When there are no longer any circulating `m1` mutations, the model outputs some final analysis and terminates. The final analysis here is in two parts. The first part simply calculates the fraction of all chromosome positions in all genomes that derives from `p1`. In one run of this model, the output happens to be:

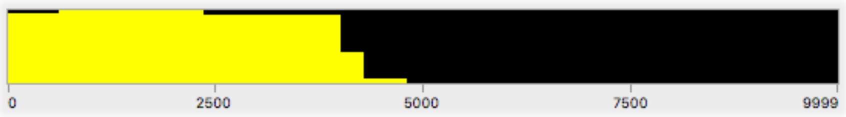
```
Fraction with p1 ancestry: 0.398137
```

The second part calculates the fraction of all genomes derived from `p1` at each individual position along the chromosome, and outputs those fractions as a big vector:

```
Fraction with p1 ancestry at each chromosome position:
0.946 0.946 0.946 0.946 0.946 0.946 0.946 0.946 0.946 0.946 0.946 0.946...
```

It does that by looping through the genomes of `p3`, and for each genome getting the positions at which `m2` mutations exist using `positionsOfMutationsOfType()`. Those vectors of positions can be converted into `integer` vectors that have a `1` at the positions where `m2` mutations occurred (and a `0` everywhere else), using the `integer()` function of Eidos. Summing those vectors across all of the `p3` genomes gives a count of the number of `m2` mutations at each position; dividing that by the maximum possible count gives a frequency, which indicates the pattern of ancestry.

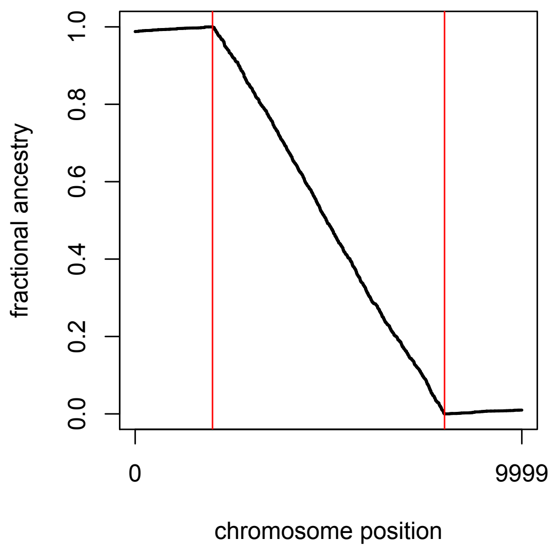
This pattern can also be seen in SLiMgui, with the neutral marker mutations shown in yellow:



This indicates that the left-hand half of the chromosome mostly derives from `p1` – albeit with some variation due to multiple recombination events that created some haplotype variation – whereas the right-hand half of the chromosome derives from `p2` in all individuals.

The recipe here tracks true local ancestry down to the level of individual base positions. This does involve some overhead, in terms of both memory usage and processor power, so if this level of granularity is not needed, it would be much more efficient to place marker mutations every 10, 100, or even 1000 positions along the chromosome. This could be done with a few trivial modifications to the recipe presented here. However, this recipe can be scaled up to $L = 1$ Mbp and still run in only a couple of minutes, so the overhead is really not too bad. For even larger models, however, both the runtime and the memory usage of this recipe can become prohibitive; at $L = 10^8$, the memory usage of this recipe is estimated to be over 8 TB (that is not a typo). Tree-sequence recording, added in SLiM 3, can provide a far more efficient alternative (see section 1.7 and chapter 16).

A final note: having done one run of the recipe and seen the pattern of ancestry in SLiMgui, it would be natural to wonder what the *average* pattern of ancestry would be across many runs. That is straightforward to do, by simply running the model many times, collecting the data from each run, and averaging the ancestry pattern across the runs. A simple R script to do this is provided in the online SLiM-Extras repository, in the "sublaunching" folder since it illustrates how to sublaunch runs of SLiM from a script (in this case, an R script). The script is named aggregateLocalAncestry.R (https://github.com/MesserLab/SLiM-Extras/blob/master/sublaunching/aggregateLocalAncestry.R). If you have R installed you should be able to run it easily, after modifying the file paths in the script to point to your installed `slim` and your copy of this recipe. If you do that, you will get a plot:



The locations where the beneficial mutations were placed in `p1` and `p2` are shown with red lines. The mean true local ancestry (the fraction of the genomes in `p3` that derive from `p1` at a given chromosome position) is exactly `1.0` at the first beneficial mutation's location, and exactly `0.0` at the second's; this makes sense, since the model did not terminate until both beneficial mutations had fixed, which would imply pure `p1` or `p2` ancestry at those positions. In between, the local ancestry changes linearly from `p1` to `p2`; it might seem plausible that the pattern would be sigmoid instead, but apparently it is not. Toward the ends of the chromosomes, outside the beneficial mutations, the ancestry falls toward `0.5`; it's hard to see here, but that fall-off is not linear, in fact. This pattern presumably recapitulates known results from population genetics, but a modified version of this model could explore much more complex scenarios.

13.10 A quantitative genetics model with heritability

Section 13.1 presented a recipe for a quantitative genetics model in which phenotype was calculated as the additive effect of a set of QTLs, and fitness was determined by individual phenotype compared to a phenotypic optimum. In this section we will extend this type of quantitative genetics model to incorporate heritability, generated by adding random deviations (representing environmental variance) to the additive genetic variation of the QTLs. Rather than extending the model of section 13.1 directly, however, we will develop a somewhat different model here. This recipe utilizes QTLs with effect sizes drawn from a continuous Gaussian distribution, rather than the `-1`/`+1` effect size distribution of section 13.1. The genetic structure here, unlike the earlier recipe, is not predetermined; new QTLs can arise spontaneously at any location. This recipe has only a single subpopulation, and does not contain assortative mating.

The mechanics of this model are quite simple. Here is the entire model except the final output event and the implementation of heritability:

```
initialize() {
    initializeMutationRate(1e-6);
    
    initializeMutationType("m1", 0.5, "f", 0.0);       // neutral
    initializeMutationType("m2", 0.5, "n", 0.0, 1.0);  // QTL
    m2.convertToSubstitution = F;
    
    initializeGenomicElementType("g1", c(m1, m2), c(1, 0.01));
    initializeGenomicElement(g1, 0, 1e5 - 1);
    initializeRecombinationRate(1e-8);
}
1 late() {
    sim.addSubpop("p1", 1000);
}
1: late() {
    // construct phenotypes from the additive effects of QTLs
    inds = sim.subpopulations.individuals;
    inds.tagF = inds.sumOfMutationsOfType(m2);
}
fitness(m2) {
    return 1.0;   // QTLs are neutral; fitness effects are handled below
}
fitness(NULL) {
    return 1.0 + dnorm(10.0 - individual.tagF, 0.0, 5.0);  // optimum +10
}
```

Section 13.1 explained the mode of operation of this type of model in some detail. In brief, QTLs are here represented by mutation type `m2`, and the selection coefficient of `m2` mutations is used as the additive genetic value of the QTL. A `fitness(m2)` callback makes all `m2` mutations be neutral regardless of these selection coefficients. A `fitness(NULL)` callback (a so-called "global `fitness()` callback" because it evaluates overall individual fitness, rather than the fitness of a focal mutation) returns a fitness value that depends upon the phenotype as compared to a phenotypic optimum of `10.0`, using a Gaussian function as in many such models.

Note that, as in section 13.1, a baseline value of `1.0` is added to the Gaussian function value returned by `dnorm()`. Section 13.1 didn't really discuss that choice in any detail, however; let's embark on that digression now. Fundamentally, the problem is that of trying to choose a function that provides a reasonable phenotype-to-fitness map. There is not a lot of empirical data to guide this choice in most systems, so it is a difficult and somewhat arbitrary decision. In a hard selection model, where low mean population fitness results in a decrease in population size, an appropriate fitness function might have a minimum value of zero, allowing the modeling of phenomena such as lethal mutations and population extinction. In such a model, if most individuals have a fitness of `0.001` and one has a fitness of `0.1` (having just received a beneficial mutation, for example), most of the individuals will produce no offspring at all, while the individual with fitness of `0.1` might produce just one or two, leading to a very small population in the next generation. This seems quite reasonable. The same situation in a soft selection model, where population size does not depend upon mean population fitness, makes considerably less sense, however. In this scenario, the child generation must be filled with the requisite number of individuals, so the individual with fitness `0.1` will end up generating most of the offspring – perhaps hundreds or even thousands of offspring – while all the rest of the individuals survive but generate few or no offspring. For some organisms this might be realistic, but for many it would be nonsensical – no matter how much more fit one elephant is than all of the other elephants in Africa, it is not going to generate thousands of offspring all across Africa all by itself! In short, fitness in soft selection models works differently than in hard selection models, and is often modeled more appropriately with a fitness function that does not allow such large differences in relative fitness to exist, so that one individual does not completely dominate the reproductive output of the population. Adding a constant value to a Gaussian function is a simple way to achieve this; the larger the constant added, the more the relative fitness values in the population are effectively homogenized. Using a constant of `1.0` makes some superficial sense, since `1.0` represents neutrality and the Gaussian function can then be thought of as being some marginal increase in fitness beyond neutrality. However, this constant is actually arbitrary; after the rescaling that is implicit in the concept of relative fitness, `1.0` will not be neutral anyway. The constant added should probably therefore be considered to be a free parameter of the model, if a fitness function of this form is used.

To continue this digression a bit longer, it is also worth noting that if large differences in relative fitness are allowed in a model, as with the situation above where most individuals have fitness `0.001` and one has fitness `0.1`, this can lead to undesirable mate-choice dynamics, too. By default, SLiM models are hermaphroditic, and while they employ biparental mating by default, they do not prevent the same parent from being chosen as *both* parents in a biparental mating event, resulting in hermaphroditic selfing. Normally this is not a problem, since for typical population sizes it is unlikely to occur often enough to make a significant difference to the model's results. In some sense it is even desirable, since this behavior means that SLiM's default configuration mirrors simple analytical population genetics models more closely; this is the reason why SLiM does not prevent it by default. However, when there is large variance in fitness or when the effective population size is very small, the chance of hermaphroditic selfing can become quite high; the fitness `0.1` individual may be quite likely to be chosen as both parents of a given offspring, and it may therefore generate most of its offspring through selfing. In that case it may be desirable to suppress it. See section 12.4 for further discussion of this issue and how to deal with it in SLiM.

Returning from that digression: In this model, phenotypes are calculated as the sum of the effects of all of the QTLs possessed by each individual, and are stored in the `tagF` property of individuals for use within the global `fitness()` callback. The core calculation is done here by the `sumOfMutationsOfType()` method, which loops over all of the mutations in each individual and sums up the selection coefficients of all of the mutations of type `m2`, which represent the QTLs possessed by the individual. The sum of the selection coefficients of those mutations represents the total of the additive effects of the QTLs. These result values – calculated phenotypes – are assigned into the `tagF` property of the individuals. Note that this implementation produces a codominant model; each QTL allele possessed has the same additive effect. It would be possible to implement a dominant QTL model; it would require replacing the `sumOfMutationsOfType()` call with method calls to get the mutations possessed by each individual with `mutationsOfType()`, unique them with `unique()`, get their selection coefficients, and total them up with `sum()`. This can be done in one line for the whole vector of individuals, using `sapply()`, but is not shown here.

QTLs are about 1% of all new mutations, and thus new QTLs arise spontaneously throughout the run. If they tend to improve the phenotypes of individuals in the population, then they tend to be retained; if not, they tend to be lost. The population as a whole begins with a mean phenotype of `0.0`, since no QTLs exist. Over the model run, the population will execute an adaptive walk towards the fitness peak at `+10.0`. The only other component we need for the base model is an event that checks for the termination condition (arrival at the fitness peak) and prints output:

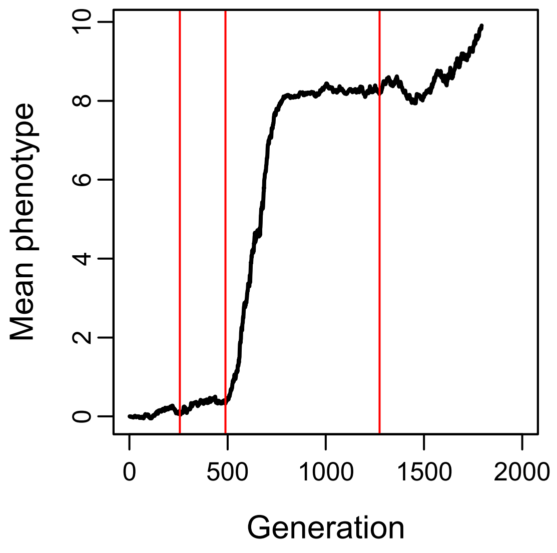
```
1:100000 late() {
    if (sim.generation == 1)
       cat("Mean phenotype:\n");

    meanPhenotype = mean(p1.individuals.tagF);
    cat(format("%.2f", meanPhenotype));

    // Run until we reach the fitness peak
    if (abs(meanPhenotype - 10.0) > 0.1)
    {
       cat(", ");
       return;
    }

    cat("\n\n-------------------------------\n");
    cat("QTLs at generation " + sim.generation + ":\n\n");

    qtls = sim.mutationsOfType(m2);
    f = sim.mutationFrequencies(NULL, qtls);
    s = qtls.selectionCoeff;
    p = qtls.position;
    o = qtls.originGeneration;
    indices = order(f, F);

    for (i in indices)
       cat("   " + p[i] + ": s = " + s[i] + ", f == " + f[i] +
          ", o == " + o[i] + "\n");

    sim.simulationFinished();
}
```

This event runs in every generation. It prints the mean phenotype in each generation, forming a comma-separated list that can be easily copied into an environment such as R for plotting. When the fitness peak is reached, within a small tolerance, it prints a list of all of the QTLs in the population and terminates. The QTL list contains the position, effect size, frequency, and origin generation of each QTL, and is sorted by frequency using the `order()` function.

A run of the model produces output like this:

```
Mean phenotype:
0.00, -0.00, -0.00, -0.01, -0.00, -0.00, -0.01, -0.01, -0.01, -0.01, ...,
9.77, 9.77, 9.82, 9.81, 9.83, 9.83, 9.84, 9.85, 9.85, 9.82, 9.89, 9.91

-------------------------------
QTLs at generation 1793:

   45907: s = 1.28919, f == 1, o == 489
   98721: s = 2.78947, f == 1, o == 257
   53961: s = 1.59969, f == 0.592, o == 1274
   21414: s = -1.09245, f == 0.0515, o == 1639
   93840: s = -0.338536, f == 0.0345, o == 1657
   74095: s = 1.35625, f == 0.026, o == 1762
   ...
```

Plotting the mean phenotype time series in R produces a visualization of the adaptive walk:



The black curve shows the mean phenotype over time; the three red lines show the generations of origin of the three high-frequency QTLs listed in the output above. This visualization shows that the adaptive walk involved a joint sweep by the first two QTLs, followed by a second sweep by the third QTL, which arose later. At the end of the run, the population has reached the adaptive peak only on average, since the third QTL is present at a frequency of only 0.592. Individuals that do not possess this QTL at all have a phenotype of ~8.16; those with only one copy have a phenotype of ~9.76; and those with two copies have a phenotype of ~11.36. In the final state of the model, heterozygote advantage thus produces balancing selection upon the third QTL.

So far so good; but earlier it was promised that this model would incorporate heritability as well. Let's add that now, beginning with the addition of a line at the top of the `initialize()` callback that sets up a constant representing the desired heritability, h^2:

```
defineConstant("h2", 0.1);
```

And then, here is a complete replacement for the `1: late()` event that calculates phenotypes:

```
1: late() {
    // construct phenotypes from the additive effects of QTLs
    inds = sim.subpopulations.individuals;
    tags = inds.sumOfMutationsOfType(m2);

    // add in environmental variance, according to the target heritability
    V_A = sd(tags)^2;
    V_E = (V_A - h2 * V_A) / h2;    // from h2 == V_A / (V_A + V_E)
    env = rnorm(size(inds), 0.0, sqrt(V_E));

    // set phenotypes
    inds.tagF = tags + env;
}
```

This replacement event calculates phenotypes in much the same way as the original, but with the addition of random noise representing environmental variance. The desired environmental variance is calculated based upon the additive genetic variance and the heritability, following standard quantitative genetics, and `rnorm()` is used to generate random values with (approximately) the desired variance.

The model above produces somewhat different results than the original model without heritability. The most obvious difference is that the plot of mean phenotype over time is noisier, because the mean phenotype itself is noisier. Other effects of the heritability on the evolutionary trajectory are more difficult to see in a single run; statistical analysis of a large number of runs would be needed to draw firm conclusions.

We have often used the term "phenotype" here, rather than just referring to, e.g., the breeding value of the quantitative trait. This is deliberate, because this model really is a model of selection on the organism phenotype. Here the phenotype is determined by just a single quantitative trait, but it would be quite simple to extend the model to encompass multiple traits that all influenced the organism's phenotype in different ways. The `1: late()` event here encapsulates the genotype-to-phenotype map, and can be broadened to any such map desired, for any number of traits. In this model, the global `fitness()` callback defines the phenotype-to-fitness map according to the Gaussian fitness function used there. In a model in which phenotype encompassed multiple traits, the definition of the phenotype-to-fitness map would probably move to the `1: late()` event as well, and the final fitness effect of the whole phenotype would be stored in `tagF`; the global `fitness()` function would then simply return the `individual.tagF` fitness value previously stored.

It should be noted that this model demonstrates just one possible way of adding environmental variance to influence heritability. The method used here does not change the magnitude of the additive genetic variance, and so the overall phenotypic variance will be larger with lower heritability. Alternatively, one could scale the additive genetic variance down so that the phenotypic variance remains constant regardless of the heritability value chosen. Both methods would achieve the same target heritability value, but with different overall phenotypic variance.

In fact, trying to attain a target heritability value, as done here, is rather artificial to begin with; it is common in analytical quantitative genetics models, but from an individual-based perspective such as that of SLiM, the heritability is properly regarded as an emergent property of the model, not a value the model should impose. From that perspective, the better approach would be to simply add in environmental variation of a particular magnitude (determined from empirical data, perhaps). The magnitude of the environmental variance, rather than the heritability, would be the model parameter, and the heritability would be a consequence of the model's dynamics. The code above can of course be easily modified to implement such a scheme instead.

It should also be noted that in this model the heritability being modeled is both the narrow-sense heritability h^2 and the broad-sense heritability H^2; they are the same here, because V_A is equal to V_G, which is true because the only source of genetic variance is the additive effects of the QTLs. If that were no longer the case (due to epistasis, maternal effects, dominance, etc.), then the model might need to be modified to correctly implement the particular type of heritability desired; that gets into quantitative genetics theory that we will not explore further here.

The heritability algorithm used here is adapted from code kindly provided by Mikhail Matz.

13.11 Live plotting with R using system()

The previous section presented a final analysis of the results from its recipe using a plot generated in R after the model had finished. SLiMgui provides some built-in plots, as we saw in chapter 8, but it would be awfully nice to be able to make custom plots through R's extensive plotting facilities within a running SLiM model – and even better, to have those plots update live as the model runs in SLiMgui. That is the goal of this section's recipe.

To achieve this goal, we will use several tools we haven't encountered before now. Most important is the Eidos `system()` function, which allows any Un*x command to be executed; we will use it to sublaunch R processes that will generate plots for us. We will also use the Eidos `writeTempFile()` function, which facilitates the generation of temporary files with unique, noncolliding filenames; we will use it to create both the R script we will execute and the PDF plot file we will display. Let's launch into it:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
```

Just a vanilla neutral model setup, nothing surprising. Next is the generation `1` setup:

```
1 {
    sim.addSubpop("p1", 5000);
    sim.setValue("fixed", NULL);

    defineConstant("pdfPath", writeTempFile("plot_", ".pdf", ""));

    // If we're running in SLiMgui, open a plot window
    if (exists("slimgui"))
      slimgui.openDocument(pdfPath);
}
50000 late() { sim.outputFixedMutations(); }
```

In generation `1`, we create a new subpopulation as usual. We also start a new value kept by the simulation, named `fixed`; this will keep a record of the number of fixed mutations over time as the simulation runs, and that is what we will plot.

Next we call `writeTempFile()` to make a temporary file with a filename that begins with `"plot_"` and ends with `".pdf"`; several characters in between will be randomly generated by `writeTempFile()` to create a unique filename that is not presently used in the `/tmp/` directory where the file will be placed. This call returns the filesystem path to the file it creates, and we define that as a constant named `pdfPath` for future use.

The last couple of lines execute only if the model is running in SLiMgui; when running at the command line, the `slimgui` object does not exist. When running in SLiMgui, on the other hand, `slimgui` is a global singleton object (of Eidos class `SLiMgui`) that represents the SLiMgui application itself, and can be used to control SLiMgui from a model's script (see section 21.11). If the `slimgui` object exists, as tested by the Eidos function `exists()`, then we are indeed running in SLiMgui, in which case we call the `openDocument()` method of `slimgui` with the path to the PDF file we have just created. A new window should open in SLiMgui as a result; initially it will be blank since the PDF file is empty, but it will update automatically whenever the PDF file changes.

Since we are running in SLiMgui, we can rely upon it for the automatically updating PDF display facility used here. Note that users running SLiM at the command line in Linux could presumably do something very similar to open the plot file in the PDF preview app of their choice, and get live plotting even without running SLiMgui. This could probably be done, for example, with a call to the Eidos function `system()` to request the operating system to open the PDF file in the user's preferred application; on macOS a command named `open` exists to perform such tasks, so presumably something similar exists on Linux. (If a Linux user reads this and figures out how to do this in a general way, please let us know and we'll document it here). Note, however, that many PDF display programs do not notice when the file changes, and will not automatically redisplay it.

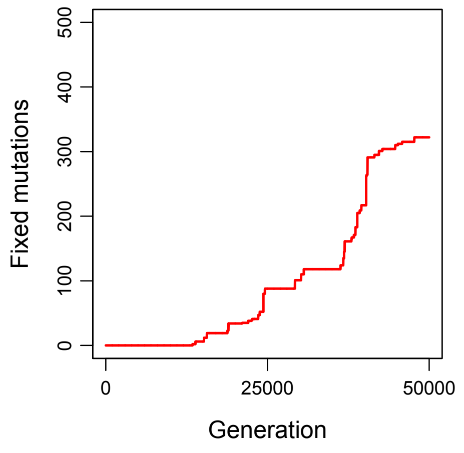
Finally, we have a generation `50000` event that ends the simulation. All we need in addition to that code is an event to tabulate results and generate plots:

```
1: {
    if (sim.generation % 10 == 0)
    {
       count = sim.substitutions.size();
       sim.setValue("fixed", c(sim.getValue("fixed"), count));
    }
    
    if (sim.generation % 1000 != 0)
       return;
    
    y = sim.getValue("fixed");
    
    rstr = paste(c('{',
       'x <- (1:' + size(y) + ') * 10',
       'y <- c(' + paste(y, sep=", ") + ')',
       'quartz(width=4, height=4, type="pdf", file="' + pdfPath + '")',
       'par(mar=c(4.0, 4.0, 1.5, 1.5))',
       'plot(x=x, y=y, xlim=c(0, 50000), ylim=c(0, 500), type="l",',
          'xlab="Generation", ylab="Fixed mutations", cex.axis=0.95,',
          'cex.lab=1.2, mgp=c(2.5, 0.7, 0), col="red", lwd=2,',
          'xaxp=c(0, 50000, 2))',
       'box()',
       'dev.off()',
       '}'), sep="\n");
    
    scriptPath = writeTempFile("plot_", ".R", rstr);
    system("/usr/local/bin/Rscript", args=scriptPath);
}
```

First of all, every tenth generation we add the current count of fixed mutations to the value we're using to tabulate those results, using `getValue()` and `setValue()` to update the saved value.

Second, every 1000th generation we generate a new plot. First, we get the current tabulation of counts using `getValue()`. Then we assemble an R script into `rstr` using a rather complicated command that spans twelve lines. A call to `c()` is used to piece together a vector of script lines, some of which are simple strings, others of which are themselves assembled using the + operator to concatenate strings and so forth. The vector of script lines is then pasted together using a newline character as the separator, to make a more or less readable R script (you could add a print() call to see the final result if you wish). We write that script to a temporary file using writeTempFile(), and then we call system() to request that `Rscript` should run our script. (`Rscript` is a command-line utility for running R scripts, typically installed as part of a standard R installation; see the R documentation for more information on it.)

That is all that is needed. SLiMgui will automatically notice that the PDF file has been overwritten with new data, and will redisplay it more or less continuously (there is a short lag because of delays involved in filesystem notifications and other factors, but typically less than a second). At the end of a typical run, the plot window in SLiMgui shows something like this:



The plotting code that we sent to R included niceties like axis labels, font sizes, and line colors, so the final plot is reasonably nice-looking. Beyond aesthetics, we can see a few interesting things in this plot. First of all, there is a long delay – perhaps 15000 generations – before any mutations fix at all. This is because the chromosome starts empty, in this model, and it takes some time to accumulate neutral diversity and have it drift to fixation. This is why it is usually important to run models for a burn-in period before collecting data, of course; the early state of a model is usually far from equilibrium. Second, even after mutations start to fix the line is quite jagged; there are long periods without any fixation, and then sudden jumps when many mutations fix simultaneously. This is because whole haplotypes representing many individual mutations often fix as a single unit, followed by periods in which competing haplotypes are drifting up and down in frequency without fixation; these dynamics are also very visible in SLiMgui's chromosome view.

Apart from a little bit of hassle involved in assembling an R script as an Eidos string, this recipe is quite short and simple considering that it is continuously writing new script files and then sublaunching R processes to generate PDF plots! This example is quite simple, but there is no limit to the complexity possible here; arbitrary plots could be made, multiple plots could be generated simultaneously, and other processing, such as statistical analysis, could be done in R.

13.12 Modeling nucleotides at a locus

SLiM provides no intrinsic support for explicitly modeling the nucleotide sequence along the chromosome. In general, such models are conceptually quite different from SLiM; they tend to be concerned with the probability that each ATGC base will mutate into each other type of base, and use Markov models and similar constructs to model changes to the nucleotide sequence as realistically as possible, for the purpose of, for example, accurately calculating divergence time using molecular data, or calculating a maximum likelihood phylogeny given sequence data. They also often concern themselves with things like codons and amino acids, codon degeneracy, synonymous and nonsynonymous mutations, stop codons, nonsense mutations, and so forth, for example to model the evolution of protein sequences. None of those concepts is really within SLiM's domain, and although in principle they could all be modeled in script, at some point the question arises as to whether, for driving in a screw, a better tool than a hammer might exist.

Nevertheless, in some cases it is desirable to model in SLiM the possibility that a given base position can take on exactly one of four distinct values, representing nucleotides, while ignoring the aforementioned issues involved in more realistic modeling of nucleotide sequences. This could be useful if, for example, it is important that a given base position can possess only four possible discrete fitness effects – that there be just four distinct alleles at that location. It could also be important for models in which back-mutation is important, such that a new mutation that arises at a given location leads to the previous allelic state with a one-in-three chance.

This is possible to model in SLiM, using a little bit of scripting to modify SLiM's default behavior. Here we will look at one strategy for doing so.

To begin with, here is the `initialize()` callback we will use to set up the simulation:

```
initialize() {
    defineConstant("C", 10);      // number of loci

    // Create our loci
    for (locus in 0:(C-1))
    {
      // Effects for the nucleotides ATGC are drawn from a normal DFE
      effects = rnorm(4, mean=0, sd=0.05);

      // Each locus is set up with its own mutType and geType
      mtA = initializeMutationType(locus*4 + 0, 0.5, "f", effects[0]);
      mtT = initializeMutationType(locus*4 + 1, 0.5, "f", effects[1]);
      mtG = initializeMutationType(locus*4 + 2, 0.5, "f", effects[2]);
      mtC = initializeMutationType(locus*4 + 3, 0.5, "f", effects[3]);
      mt = c(mtA, mtT, mtG, mtC);
      geType = initializeGenomicElementType(locus, mt, c(1,1,1,1));
      initializeGenomicElement(geType, locus, locus);

      // We do not want mutations to stack or fix
      mt.mutationStackPolicy = "l";
      mt.mutationStackGroup = -1;
      mt.convertToSubstitution = F;

      // Each mutation type knows the nucleotide it represents
      mtA.setValue("nucleotide", "A");
      mtT.setValue("nucleotide", "T");
      mtG.setValue("nucleotide", "G");
      mtC.setValue("nucleotide", "C");
    }

    initializeMutationRate(1e-6);   // includes 25% identity mutations
    initializeRecombinationRate(1e-8);
}
```

First of all, note that the length of the chromosome is a defined constant, `C`, but here we will work with just `10` bases just to keep the output simple. This recipe will work for longer chromosomes too, although there is a price paid in speed and memory usage.

The initialization code loops over the loci, from `0` to `C-1`, and sets up each locus with its own mutation types, genomic element type, and genomic element. Each locus will have four nucleotides, ATGC, each of which has a random fitness effect; those effects are drawn from a normal distribution using `rnorm()`. The code creates a mutation type for each nucleotide type, each using one of the fixed selection coefficients drawn. In other words, each nucleotide type gets its own mutation type at each locus; since this recipe contains `10` loci, there will be `40` mutation types in all. A genomic element type is created using those four mutation types in equal proportions (different proportions could be used if mutational bias is desired), and a genomic element at the locus in question is created using that genomic element type.

We want new mutations to replace the old mutation at a locus, since that is how nucleotides work (a base position is never two nucleotides at the same time), so we set `mutationStackPolicy` and mutationStackGroup accordingly. By setting all of the mutation types to the same mutationStackGroup, nucleotides will all replace each other; there will be no mutation stacking in this model. We never want these mutation types to fix – this model will never allow a locus to be empty (as normally occurs in SLiM), since a base position is always either A,T, G, or C – so we set convertToSubstitution to F. Finally, we use setValue() to save each mutation type's nucleotide under the name "nucleotide" for later reference; this is only for purposes of output (note that it would be more memory-efficient to use integer values of the tag property of the mutation types to represent the nucleotides instead, but would be less clear for presentation here).

Next, the initialize() callback sets the mutation rate. Note that in this model a nucleotide can mutate into itself; an A can mutate to become an A, a T to become a T, etc. This is not prohibited because the mutation-generation machinery in SLiM generates new mutations without reference to what mutation might already exist at that locus. The mutation rate specified for this model is therefore higher than the "real" mutation rate will be; approximately 25% of mutations will be no-ops that do not change the existing nucleotide.

Finally, the recombination rate is set. This recipe models a linked string of ten nucleotides; to model ten unlinked loci instead, a recombination rate of 0.5 could be used.

Next, we need to create an initial population:

```
1 late() {
    sim.addSubpop("p1", 2000);

    // The initial population is fixed for a single wild-type
    // nucleotide fixed at each locus in the chromosome
    geTypes = sim.chromosome.genomicElements.genomicElementType;
    mutTypes = sapply(geTypes, "sample(applyValue.mutationTypes, 1,
      weights=applyValue.mutationFractions);");
    p1.genomes.addNewDrawnMutation(mutTypes, 0:(C-1));

    cat("Initial nucleotide sequence:");
    cat(" " + paste(mutTypes.getValue("nucleotide")) + "\n\n");
}
```

The first step is, as usual, a call to addSubpop(). Then we need to set up each locus with an initial nucleotide. To do that, we first get a vector of the genomic element types for each genomic element (and thus for each base position, since we have one genomic element per base position). These genomic element types determine the candidate mutation types for each position, so we can use sapply() to draw one of the mutation types from each genomic element type, according to the probabilities specified by the genomic element type; this gives us a vector of mutation types to use for each base position. Finally, we add all of the new mutations with a single vectorized call to addNewDrawnMutation(). This design is far faster than adding the new mutations one by one in a loop. In short, this code chooses a random nucleotide sequence; it then prints out the chosen sequence using cat(). For example, this code might output:

```
Initial nucleotide sequence: C G T T A A G G A G
```

Next, we need to deal with a small issue in our scheme. Because a mutation to the same nucleotide at the same position can happen multiple times independently, even within one generation, multiple mutations representing the same nucleotide can be circulating in the population; a locus might be fixed for G, for example, but that might be represented in SLiM by 82% of genomes having one G mutation, 17% having another, and 1% having a third G mutation, all with the same selection coefficient and mutation type. This gives SLiM itself no difficulties, but depending upon the assumptions made in the rest of the model's script, it could be undesirable, at least for purposes of output. This next chunk of code is optional, but many models will want to include it for this reasons. It looks for such duplicates and fixes them, in each generation:

```
2: late() {
    // optionally, we can unique new mutations onto existing mutations
    // this runs only in 2: - it is assumed the gen. 1 setup is uniqued
    allMuts = sim.mutations;
    newMuts = allMuts[allMuts.originGeneration == sim.generation];

    if (size(newMuts))
    {
       genomes = sim.subpopulations.genomes;
       oldMuts = allMuts[allMuts.originGeneration != sim.generation];
       oldMutsPositions = oldMuts.position;
       newMutsPositions = newMuts.position;
       uniquePositions = unique(newMutsPositions, preserveOrder=F);
       overlappingMuts = (size(newMutsPositions) != size(uniquePositions));

       for (newMut in newMuts)
       {
          newMutLocus = newMut.position;
          newMutType = newMut.mutationType;
          oldLocus = oldMuts[oldMutsPositions == newMutLocus];
          oldMatched = oldLocus[oldLocus.mutationType == newMutType];

          if (size(oldMatched) == 1)
          {
             // We found a match; this nucleotide already exists, substitute
             containing = genomes[genomes.containsMutations(newMut)];
             containing.removeMutations(newMut);
             containing.addMutations(oldMatched);
          }
          else if (overlappingMuts)
          {
             // First instance; it is now the standard reference mutation
             oldMuts = c(oldMuts, newMut);
             oldMutsPositions = c(oldMutsPositions, newMutLocus);
          }
       }
    }
}
```

This gets all of the new mutations in the simulation, using `originGeneration`. It then gathers information about the pre-existing mutations, the new mutations, and their positions. Then, for each new mutation, it determines whether there is a pre-existing mutation with the same position and type; if so, it substitutes the pre-existing mutation for the new mutation in every genome.

The only twist is that when there is no pre-existing mutation, the new mutation needs to become the new "canonical" mutation for its position and type, and so it needs to be added to the vector of pre-existing mutations. This only really needs to be done if more than one new mutation exists at the same position, however, as it will only matter if a second new mutation comes along, in the same generation, that matches the first; in that case, the first needs to be used as the pre-existing mutation to replace the second. Detecting the necessity of this case is the purpose of the `overlappingMuts` flag; it allows us to skip updating the list of pre-existing mutations in most cases. (If the length of the chromosome, `C`, is increased to a large number like `10000` or more, this optimization actually makes a substantial difference to the runtime of the recipe.)

There is only one more step, which is to output something about the final state of the model:

```
10000 late() {
    muts = p1.genomes.mutations;   // all mutations, no uniquing
    
    for (locus in 0:(C-1))
    {
       locusMuts = muts[muts.position == locus];
       totalMuts = size(locusMuts);
       uniqueMuts = unique(locusMuts);
       
       catn("Base position " + locus + ":");
       
       for (mut in uniqueMuts)
       {
          // figure out which nucleotide mut represents
          mutType = mut.mutationType;
          nucleotide = mutType.getValue("nucleotide");
          cat("   " + nucleotide + ": ");
          
          nucCount = sum(locusMuts == mut);
          nucPercent = format("%0.1f%%", (nucCount / totalMuts) * 100);
          
          cat(nucCount + " / " + totalMuts + " (" + nucPercent + ")");
          cat(", s == " + mut.selectionCoeff + "\n");
       }
    }
}
```

This code loops through the loci and prints out the fraction (if any) of each nucleotide at that locus. For example, it might print:

```
Base position 0:
   C: 4000 / 4000 (100.0%), s == -0.0918891
Base position 1:
   T: 4000 / 4000 (100.0%), s == 0.0157156
Base position 2:
   T: 4000 / 4000 (100.0%), s == 0.0301955
Base position 3:
   T: 4000 / 4000 (100.0%), s == 0.0325203
Base position 4:
   C: 4000 / 4000 (100.0%), s == -0.0183944
Base position 5:
   A: 4000 / 4000 (100.0%), s == 0.0376738
Base position 6:
   G: 4000 / 4000 (100.0%), s == -0.0226032
Base position 7:
   G: 3103 / 4000 (77.6%), s == 0.0413104
   C: 897 / 4000 (22.4%), s == 0.0477822
Base position 8:
   A: 4000 / 4000 (100.0%), s == -0.0814816
Base position 9:
   C: 4000 / 4000 (100.0%), s == 0.0666566
```

This shows us that position 7 appears to be caught in mid-sweep, with a superior C nucleotide replacing the existing G nucleotide. All of the other loci are fixed for one nucleotide. We can compare this output to the initial output:

```
Initial nucleotide sequence: C G T T A A G G A G
```

The comparison indicates that the model has undergone complete substitution at positions 1, 4, and 9, in addition to the ongoing sweep at position 7 which may or may not complete.

This design allows each nucleotide to have its own dominance coefficient, providing for a fair amount of flexibility in the evaluation of fitness effects. If more complex dominance interactions are needed, in which each possible pair of homologous nucleotides could have a different arbitrary fitness value, that could be implemented by first making the mutation types intrinsically neutral, and then writing a global `fitness(NULL)` callback that examines the nucleotides at the locus in question and returns the overall fitness effect.

On the flip side, a purely neutral model of nucleotide evolution would not need separate mutation types for each locus at all; just four mutation types, representing A, T, G, and C, could be used for the whole model. This is a very easy modification of the recipe, and should be considerably more memory-efficient. A hybrid model in which neutral nucleotides are represented by four standard ATGC mutation types, while non-neutral nucleotides get their own mutation types, should also be possible; or `setSelectionCoefficient()` could probably be used.

As mentioned above, modeling explicit nucleotides could probably be done in a variety of ways. This recipe should be fairly efficient, provides quite a bit of flexibility in fitness assessment, and makes no assumptions regarding the fitness effects of nucleotides; it works just as well modeling neutral drift of nucleotides, in fact. In models of explicit nucleotides such as this, fundamentally there has to be some way of telling what nucleotide a given mutation represents. This recipe uses the mutation type to make that distinction, which is ultimately why there are four mutation types per locus. It is tempting to try to differentiate nucleotides using the `tag` property of mutations instead, setting the initial `tag` value of new mutations in a `late()` callback similar to the `2:` callback shown here. However, the present recipe should be suitable for most purposes.

13.13 Modeling haploid organisms

SLiM models diploid individuals that contain two haploid genomes; this is, at present, a design constraint in SLiM that cannot be modified. However, it is still possible to model haploids in SLiM quite easily with scripting, by effectively suppressing one of the two haploid genomes of each diploid individual. Section 13.6's recipe, which shows how to model X and Y chromosomes with a pseudo-autosomal region, shares some aspects of its design with the recipe shown here, but modeling haploids is actually much simpler. Similar techniques could be used to model mitochondrial DNA; to model systems such as haplodiploidy; and to model "alternation of generations", in which alternate generations in the model are diploid sporophytes and haploid gametophytes (although in many cases that might be more easily modeled using a `modifyChild()` callback to simulate selection during the haploid life stage). Here, however, we will stick with a simple model of haploids that reproduce clonally. This model is simple enough that we will just present it in its entirety, rather than building it incrementally:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 1.0, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(0);
}
1 {
    sim.addSubpop("p1", 500);
    p1.setCloningRate(1.0);
}
```

```
late() {
    // remove any new mutations added to the disabled diploid genomes
    sim.subpopulations.individuals.genome2.removeMutations();

    // remove mutations in the haploid genomes that have fixed
    muts = sim.mutationsOfType(m1);
    freqs = sim.mutationFrequencies(NULL, muts);
    sim.subpopulations.genomes.removeMutations(muts[freqs == 0.5], T);
}
200000 late() {
    sim.outputFixedMutations();
}
```

We begin with a typical `initialize()` callback, except that the recombination rate is set to zero since there is no recombination in this clonal model. Note also that although this is a neutral model for simplicity, the dominance coefficient is set to `1.0` on mutation type `m1` as a reminder; since mutations will never be homozygous in this model, dominance coefficients should always be `1.0` for conceptual clarity. Next we add a new subpopulation in generation `1` as usual; but in addition, we set the subpopulation to reproduce clonally, as befits haploids (but see section 15.14). At the end of the model we output fixed mutations, as a placeholder for whatever output would be desired. The interesting model mechanics occur in between, with the `late()` callback.

The first part of the `late()` callback removes mutations in the second haploid genome of each new child generated. SLiM doesn't know that we're modeling haploids, and thus not using the second genomes, so it adds new mutations to them as usual during offspring generation. This call removes them again in order to keep all of the second genomes of individuals empty.

The second part of the `late()` callback solves another problem: removing fixed mutations. SLiM automatically converts fixed mutations into `Substitution` objects and removes them from the simulation; however, it defines fixation as occurring when the frequency of a mutation reaches `1.0`. In this haploid model, mutations fix when they reach a frequency of `0.5`, because of the empty second genomes. We therefore need to remove mutations manually, rather than relying on SLiM's built-in machinery. This callback achieves that, passing `T` for the `substitute` parameter of `removeMutations()` so that `Substitution` objects are created for the fixed mutations as usual.

Those are the only overrides needed in script to produce a model of haploids. The mechanisms used here to enforce haploidy, such as removal of mutations on the unused chromosome and substitution of fixed mutations at a frequency of `0.5`, could also be used to make just one segment of the simulated chromosome haploid. This would allow mitochondrial DNA and autosomal DNA to be jointly simulated in SLiM, for example. Some modifications to the recipe above would be needed to achieve this; you would probably want to use a sexual autosomal model with biparental mating, add code to the `modifyChild()` callback to enforce maternal inheritance of the mitochondrial DNA (i.e., to block any proposed child that received its mitochondrial DNA from the father, or both parents, or neither), and use a recombination map to prevent recombination in the mitochondrial portion of the genome, for example. Section 13.6 provides an example of a scenario that is in many ways parallel to that. Other ploidy schemes, such as haplodiploidy and alternation of generations, should also be implementable with modifications of these basic ideas.

For an alternative model of haploid organisms that is more compatible with tree-sequence recording (chapter 16), but which requires the nonWF model type, see sections 15.13 and 15.14.

13.14 Using mutation rate variation to model varying functional density

Beginning with SLiM 2.5, it is possible to set up a mutation-rate map that varies the mutation rate along the length of the chromosome, similarly to setting up a recombination-rate map as already supported by SLiM; see sections 6.1.1 and 6.1.2, for example. This feature can, of course, be used for the obvious purpose of configuring mutational "hot" and "cold" spots along the chromosome, and the code for doing so would look much like the code for those recipes. Here, we will instead explore a less obvious use: modeling positional variation in functional density.

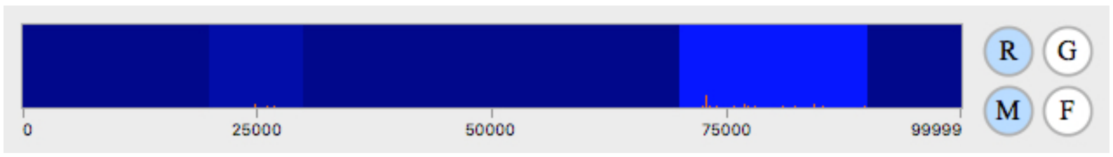
We know that different regions of chromosomes often have higher or lower functional density, as a consequence of variation in the density of genes and the importance of those genes. Regardless of the literal appropriateness of the term "junk DNA", it is clear that large chromosomal regions exist that are non-coding, and mutations in these regions generally appear to have relatively little effect on fitness compared to mutations in coding regions. This is quite orthogonal to mutational "hot" and "cold" spots; the variation we are concerned with here is not in the mutation rate *per se*, but in the rate at which mutations actually influence fitness.

Prior to SLiM 2.5, modeling this would have required that one define a complex map of genomic elements along the chromosome, all experiencing the same mutation rate (since that could not be varied), but using a different fraction of neutral mutations to deleterious mutations (and/or beneficial mutations, but for simplicity we will here focus on deleterious mutations). This design would have been necessary in order to achieve the desired variation in the rate of deleterious mutations, even if one was not actually interested in the neutral mutations at all. Such a model would run much more slowly than necessary because of the neutral mutation overhead.

By defining a mutation-rate map, however, it is now straightforward to build a model in which functional density varies along the chromosome, without having to model the neutral mutations. A proof-of-concept model for this is so simple as to be trivial:

```
initialize() {
    initializeMutationType("m1", 0.5, "f", -0.01);  // deleterious
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
    
    // Use the mutation rate map to vary functional density
    ends = c(20000, 30000, 70000, 90000, 99999);
    densities = c(1e-9, 2e-8, 1e-9, 5e-8, 1e-9);
    initializeMutationRate(densities, ends);
}
1 {
    sim.addSubpop("p1", 500);
}
200000 late() { sim.outputFixedMutations(); }
```

The variables ends and densities are set up to encode the desired mutation-rate map, with the end position for each chromosomal range and the effective functional density – the rate of mutations having a deleterious effect, in this model – of that chromosomal range. As the recipes of sections 6.1.1 and 6.1.2 illustrate, such maps can easily be generated randomly based upon empirical metrics, or can even be read in from a file with empirical map data; in this model, to keep things simple, we instead just specify a very simple map with five regions of different functional density. After the model has been initialized, clicking the Ⓡ button in SLiMgui will show the mutation-rate map (we have seen that button show the recombination-rate map before; it shows whichever map has been defined, or both if both have been defined):



The highest rate is in the region from base position 70000 to 89999, and indeed quite a few deleterious mutations can be seen in that region (but none at very high frequency; the parameters used in this model mean that the deleterious mutations are eliminated fairly efficiently). There is a somewhat less active region from 20000 to 30000, with a handful of mutations; the rest of the chromosome has a lower functional density, and receives deleterious mutations relatively rarely.

In this recipe we work with only one mutation type, modeling deleterious mutations. It would be possible to extend it to include several types of functional mutations, each with a different rate of occurrence along the chromosome. In that case, the mutation-rate map would be set to encode the sum of the rates for each of the mutation types in each chromosomal region, and genomic elements would be used to partition mutations in each region into the correct fraction for each of the functional mutation types. This would be somewhat more complex than this recipe, but manageably so; and it would again be much more efficient than using a constant mutation rate along the chromosome together with a varying fraction of neutral mutations, since modeling all of the neutral mutations could again be avoided.

13.15 Modeling microsatellites

A microsatellite (also known as a *short tandem repeat* or *simple sequence repeat*) is a chromosomal region in which a specific nucleotide sequence repeats, often many times. Microsatellites are important in many areas of applied genetics, from kinship analysis to forensics, and are also often used to assess the similarity among individuals or subpopulations in ecology and evolutionary biology. It is thus useful to be able to include them in evolutionary models. Since SLiM does not model actual nucleotides, explicitly modeling the repeated nucleotide sequence of a microsatellite doesn't fit well into its conceptual model; explicitly modeling mutations that change the number of repeats in a microsatellite would also change the length of the chromosome, which is not allowed in SLiM. Nevertheless, it is possible to model microsats more abstractly in SLiM, using mutations that conceptually represent a microsat with a particular number of repeats at a given locus. This recipe will illustrate one simple approach to this.

We will build this model step by step. First, the model initialization:

```
initialize() {
    defineConstant("L", 1e6);           // chromosome length
    defineConstant("msatCount", 10);    // number of microsats
    defineConstant("msatMu", 0.0001);   // mutation rate per microsat
    defineConstant("msatUnique", F);    // T = unique msats, F = lineages

    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);  // neutral
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, L-1);
    initializeRecombinationRate(1e-8);

    // microsatellite mutation type; also neutral, but magenta
    initializeMutationType("m2", 0.5, "f", 0.0);
    m2.convertToSubstitution = F;
    m2.color = "#900090";
}
```

We define the length of the chromosome (`L`), and several constants related to our microsats: the number of microsats we will model, the mutation rate per microsat (per genome per generation), and a flag that indicates whether to unique the microsats as the model runs (more on this below). The rest sets up a simple neutral model structure, plus a mutation type, `m2`, that will represent our microsatellites. We prevent microsatellites from fixing, with `convertToSubstitution`, since they are a permanent feature of the chromosomal structure. We also set them to display in SLiMgui using a shade of magenta, to set them apart from the other neutral mutations in the model.

Next we create a subpopulation with microsatellites:

```
1 late() {
    sim.addSubpop("p1", 500);

    // create some microsatellites at random positions
    genomes = sim.subpopulations.genomes;
    positions = rdunif(msatCount, 0, L-1);
    repeats = rpois(msatCount, 20) + 5;

    for (msatIndex in 0:(msatCount-1))
    {
       pos = positions[msatIndex];
       mut = genomes.addNewDrawnMutation(m2, pos);
       mut.tag = repeats[msatIndex];
    }

    // remember the microsat positions for later
    defineConstant("msatPositions", positions);
}
```

We call `addSubpop()` to create the subpopulation, and then we create our microsatellites. Each microsat is simply an `m2` mutation at a given position; the number of repeats in a given microsat is represented using the `tag` property of the mutation. This code draws the positions and repeats for all of the microsats first, and then loops to create each microsat using that information. Finally, we remember the positions of the microsats in a defined constant for later use.

This code makes the initial population homogenous: the number of repeats of a given microsat is the same across all genomes. It would of course be possible to start with a non-homogenous state instead. To avoid creating a new `Mutation` for every microsat in every genome, however, it would be best to determine all of the genomes containing a given repeat count at a given position, and then call `addNewDrawnMutation()` just once on that entire genome vector so as to create a single `Mutation` object that is shared among all of those genomes. Alternatively, a uniquing strategy could be employed, similar to what we will see below, such that the first microsatellite created at a given position with a given number of repeats is instantiated with a new `Mutation`, and then all subsequent microsats with the same number of repeats at the same position look up and use that existing `Mutation` object. Such extensions are left as an exercise for the reader.

With the initial subpopulation state set up, let's define an endpoint for the model:

```
10000 late() {
    // print frequency information for each microsatellite site
    all_msats = sim.mutationsOfType(m2);

    for (pos in sort(msatPositions))
    {
       catn("Microsatellite at " + pos + ":");

       msatsAtPos = all_msats[all_msats.position == pos];

       for (msat in sortBy(msatsAtPos, "tag"))
          catn("   variant with " + msat.tag + " repeats: " +
             sim.mutationFrequencies(NULL, msat));
    }
}
```

This output callback loops over the (sorted) positions of the microsats. For each microsat position, it looks up all of the microsats that exist at that position, and outputs frequency counts for each variant (sorted by repeat count).

We'll see some example output below, but the model isn't finished yet; let's finish it first. The remaining piece in the puzzle is for our microsatellites to mutate. Microsats mutate in an interesting way: they add or remove repeats. Furthermore, the probability of this happening is much higher than the usual mutation rate in most organisms – often as high as one in ten thousand. We model all this with a special `modifyChild()` callback:

```
modifyChild() {
    // mutate microsatellites with rate msatMu
    for (genome in child.genomes)
    {
        mutCount = rpois(1, msatMu * msatCount);
        
        if (mutCount)
        {
            mutSites = sample(msatPositions, mutCount);
            msats = genome.mutationsOfType(m2);
            
            for (mutSite in mutSites)
            {
                msat = msats[msats.position == mutSite];
                repeats = msat.tag;
                
                // modify the number of repeats by adding -1 or +1
                repeats = repeats + (rdunif(1, 0, 1) * 2 - 1);
                
                if (repeats < 5)
                    next;
                
                // if we're uniquing microsats, do so now
                if (msatUnique)
                {
                    all_msats = sim.mutationsOfType(m2);
                    msatsAtSite = all_msats[all_msats.position == mutSite];
                    matchingMut = msatsAtSite[msatsAtSite.tag == repeats];
                    
                    if (matchingMut.size() == 1)
                    {
                        genome.removeMutations(msat);
                        genome.addMutations(matchingMut);
                        next;
                    }
                }
                
                // make a new mutation with the new repeat count
                genome.removeMutations(msat);
                msat = genome.addNewDrawnMutation(m2, mutSite);
                msat.tag = repeats;
            }
        }
    }
    
    return T;
}
```

There's a lot to parse there; let's take it step by step. First of all, the microsats in each genome in the proposed child mutate independently, so we loop over them and mutate them separately. For each genome, we draw the number of mutations that occur from a Poisson distribution; this is faster than doing a separate random draw to determine the fate of each individual microsat, but is otherwise equivalent. If the number of microsat mutations is zero, we're done; we loop back to handle the other genome, and then we're done and return `T`. When the number of microsat mutations is greater than zero, though, we have work to do.

In that case, the next thing we do is to draw the positions of the microsats that mutated, using `sample()` to draw from the vector of positions we defined when we set up the simulation. Each microsat thus has an equal probability of mutating (see below for discussion of this). We loop over those positions and mutate each chosen microsat in turn. To mutate a microsat, we first look up the existing mutation by position and find out how many repeats it has. We then decide what the new, mutated repeat count will be; here we just add or subtract `1`, and limit the repeat count to a minimum of `5`, but more sophisticated and realistic dynamics could be introduced. Finally, ignoring the "`if (msatUnique)`" section for a moment (since msatUnique is presently defined as `F` anyway), we effect the mutation event by removing the old microsat mutation from the genome and adding a newly created microsat mutation at the same position, with the new repeat count for its tag. (We can't simply set the `tag` of the existing microsat mutation, because it is potentially shared among many genomes; changing its tag would change the repeat count in all of those genomes!)

Running this model produces output like:

```
Microsatellite at 60933:
   variant with 21 repeats: 0.001
   variant with 21 repeats: 0.026
   variant with 21 repeats: 0.001
   variant with 22 repeats: 0.741
   variant with 23 repeats: 0.105
   variant with 23 repeats: 0.126
Microsatellite at 98509:
   variant with 34 repeats: 1
Microsatellite at 123123:
   variant with 20 repeats: 0.964
   variant with 21 repeats: 0.001
   variant with 21 repeats: 0.035
Microsatellite at 142781:
   variant with 23 repeats: 0.795
   variant with 24 repeats: 0.205
...
```

This looks reasonable, except that more than one variant with the same repeat count sometimes exists for a given microsatellite. Each such variant represents an independent mutational lineage; each time a microsat mutation occurs, it is represented by a new `Mutation` object that SLiM tracks forevermore. In some cases, keeping track of each mutational lineage may be desirable; it could provide a sort of ancestry tracking, for example, that goes beyond what the repeat counts alone would provide. Often, however, one would like such replicate mutational lineages to be merged, such that just a single microsat mutation exists to represent a microsat with a given number of repeats at a given position. This is what that "`if (msatUnique)`" code, which we skipped over above, is for: it "uniques" the microsatellite lineages. To see the effect of this, let's change that flag by modifying its definition in the `initialize()` callback:

```
    defineConstant("msatUnique", T);    // T = unique msats, F = lineages
```

If we run the model again (using the same random number seed, so as to reproduce the same evolutionary dynamics), the output now looks like this:

```
Microsatellite at 60933:
   variant with 21 repeats: 0.028
   variant with 22 repeats: 0.741
   variant with 23 repeats: 0.231
Microsatellite at 98509:
   variant with 34 repeats: 1
Microsatellite at 123123:
   variant with 20 repeats: 0.964
   variant with 21 repeats: 0.036
Microsatellite at 142781:
   variant with 23 repeats: 0.795
   variant with 24 repeats: 0.205
...
```

The microsats have been uniqued, as desired. The "`if (msatUnique)`" code in the callback, which implements this feature, is actually quite straightforward. It gets a vector of all existing microsat mutations from the simulation, and then narrows that down to those at the desired position, and then finally down to those with the desired number of repeats. If it found an exact match, then it removes the existing microsat mutation and adds the match; the `next` statement then loops forward to the next mutation site, if any. If it did not find a match, the code drops through to add a newly created mutation instead; that is the case we saw before.

That's all that's needed: a little initialization code, a little output code, and a `modifyChild()` callback to handle mutating the microsats. Although that `modifyChild()` callback is not particularly short, conceptually it is really quite simple: decide on how many microsat mutation events there will be in each genome and where they will be, and then change the mutations in the genome to reflect those mutation events with new (or uniqued) mutations that have the appropriate repeat count in their `tag` values.

There are a few ways in which greater realism could be added to this model. We already discussed, above, the possibility of starting with a heterogenous subpopulation state; any initial state could be set up, although care should be taken to unique the microsat mutations, both to keep memory usage down and to provide a single mutational lineage for each unique microsatellite state.

Another way in which this model oversimplifies the biology is in its mutational model. In reality, microsats can sometimes mutate by adding or subtracting more than a single repeat, and their probability of mutating at all can depend upon the number of repeats present, as well as upon things like the sex of the parent. The mutation rate for microsats can even depend upon the similarity or dissimilarity in repeat counts between the two copies of the microsat in the parent that generated the gamete, due to effects during meiosis. All of these effects could be modeled with extensions to the `modifyChild()` callback presented here. To implement this, it would probably be necessary (or at least simpler) to get rid of the `rpois()` call that draws the number of microsat mutations for each genome, and instead simply loop over all of the existing microsat positions and determine whether a mutation occurred at each position with a `runif()` draw that is compared to the calculated probability of mutation for that microsat in that genome.

A third oversimplification is that this recipe does not explicitly track variation in microsats due to point mutations rather than repeat-count mutations. Perhaps a good approach for this would involve modeling repeat-count changes just as in this model, while adding in similar code that would model nucleotide changes as well (using an appropriate mutation probability based on the length of the microsat). If such a model was run *without* uniquing, each mutational lineage would then be tracked separately, and so point mutations would create new mutational lineages that would be considered distinct from other mutation lineages with the same repeat count. However, this design would overcount the number of genetically distinct lineages, since repeat-count mutations as well as point mutations would generate distinct mutational lineages. To account for things better would require additional state information to be attached to each `Mutation` object, using the `setValue()`/`getValue()` mechanism; in this way, two mutational lineages with the same repeat count and no nucleotide differences could be merged together by the uniquing code, while two mutational lineages with the same repeat count but *with* nucleotide differences could be kept separate. In the extreme of maximal realism, one could actually store generated `string` representations of nucleotide sequences inside the `Mutation` objects, but that would be overkill for most purposes. Usually, a single token attached to each mutation, such as a random number generated with `runif()`, could probably provide sufficient realism. Whenever a point mutation occurred, a new mutation object would be created (with no uniquing necessary) and would be given a new random token representing its unique new nucleotide sequence. Whenever a repeat-count mutation occurred, on the other hand, the token value would be inherited from the old microsat mutation at that position, indicating that the nucleotide difference, whatever it might be, was (assumed to be) preserved across the repeat count change. If the uniquing code then re-used an existing mutation only when the token values of the desired mutation and the existing mutation were the same, a closer approximation of the correct pattern of microsatellite diversity might emerge. Implementing this goes beyond the scope of this recipe, and so is left as an exercise for the reader, but in essence it is actually quite simple; the design simply adds another piece of state, tracked with `setValue()`/`getValue()`, that is handled very similarly to the `tag` value in the existing recipe. That token value is inherited (just as `tag` is), changes its value upon mutation (just like `tag`, but for point mutation events instead of repeat-count mutation events), and must be equal in order for uniquing to find a match (just as `tag` is used by the existing uniquing code). Token values would be set up when the subpopulation is initialized, just as `tag` values are, either with zero values (representing a homogenous initial state) or with some sort of population structure indicated by different random token values on different genomes to represent standing variation in microsatellite diversity.

Depending upon the level of realism desired, therefore, this recipe might provide a complete solution, or it might merely point the way. In either case, the basic strategy outlined here of using `tag` values to indicate repeat counts on mutations that represent a microsatellite at a given locus is the recommended approach in SLiM. In general, using mutations to represent some conceptual difference between genomes, rather than necessarily representing a literal nucleotide difference, can be a useful strategy for advanced models in SLiM.

13.16 Modeling transposable elements

A transposable element, or *transposon*, is a chromosomal region which is capable of replication or positional change within the genome, either on its own or with the assistance of an enzyme such as reverse transcriptase or transposase. Transposons constitute a substantial fraction of the genome of many species, and can have evolutionary effects through side effects such as disabling genes into which they "jump", altering the regulation of nearby genes, and copying genetic material within the genome. Given their evolutionary importance, incorporating transposons into evolutionary models may be useful; in this recipe we will therefore explore a simple model of transposons in SLiM.

There are various subtypes and classifications of transposons; here we will explore autonomous Class I transposons, which "copy and paste" themselves to new locations in the genome under their own power. Given the diversity of evolutionary effects transposons can have, and the diversity of ways in which they can function, this recipe cannot provide a general formula for modeling transposons and all of their effects; all this recipe will do is point the way. At the end of this section, we will discuss ways in which this recipe could be extended to model further aspects of the behavior of transposons.

Since SLiM does not model nucleotides explicitly, we will not model the actual nucleotide sequence of transposons here. Furthermore, since copying a transposon to a new location changes the length of the chromosome (which is not possible in SLiM), we will model transposons conceptually rather than literally, as loci in the genome that are capable of copying themselves. This approach is similar to the approach taken in section 13.15 for modeling microsatellites.

We will also model the vulnerability of transposons to mutations that disable them by deactivating their ability to jump; we will track disabled transposons, and assess the fraction of each transposon that has been disabled. This is important, since even disabled transposons may have evolutionary effects such as changes in gene regulation, and since most of the transposons in typical organisms appear to be disabled.

We will start with the model's initialization:

```
initialize() {
    defineConstant("L", 1e6);                  // chromosome length
    defineConstant("teInitialCount", 100);  // initial number of TEs
    defineConstant("teJumpP", 0.0001);      // TE jump probability
    defineConstant("teDisableP", 0.00005);  // disabling mut probability
    
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);  // neutral
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, L-1);
    initializeRecombinationRate(1e-8);
    
    // transposon mutation type; also neutral, but red
    initializeMutationType("m2", 0.5, "f", 0.0);
    m2.convertToSubstitution = F;
    m2.color = "#FF0000";
    
    // disabled transposon mutation type; dark red
    initializeMutationType("m3", 0.5, "f", 0.0);
    m3.convertToSubstitution = F;
    m3.color = "#700000";
}
```

This defines the chromosome length and a few constants governing the behavior of TEs in the model. It then sets up a simple neutral simulation, and defines two additional mutation types: one for active TEs, `m2`, which displays as red in SLiMgui, and one for TEs that have been disabled by mutation, `m3`, which display as a darker red.

Next we set up the initial state of our subpopulation. In this recipe, the `tag` values on the `m2` and `m3` mutations are used as identifiers; each TE gets its own unique `tag` value, which is used for both its active (`m2`) and disabled (`m3`) forms, allowing the mutations representing the two forms to be matched up. The `tag` value on the simulation itself, `sim.tag`, is used to keep track of the next unused `tag` value; it starts at `0` and counts up. The setup thus looks like this:

```
1 late() {
    sim.addSubpop("p1", 500);
    
    sim.tag = 0; // the next unique tag value to use for TEs
```

```
        // create some transposons at random positions
        genomes = sim.subpopulations.genomes;
        positions = rdunif(teInitialCount, 0, L-1);
        
        for (teIndex in 0:(teInitialCount-1))
        {
            pos = positions[teIndex];
            mut = genomes.addNewDrawnMutation(m2, pos);
            mut.tag = sim.tag;
            sim.tag = sim.tag + 1;
        }
    }
```

We make a new subpop, start `sim.tag` at `0`, and then create new TEs that are fixed across the whole population. (As in the recipe of section 13.15, creating an initial state that involves heterogeneity in the TEs possessed by individuals would also be possible but is more complex; see that recipe for discussion.) The positions for the TEs are drawn randomly across the chromosome, and each TE is tagged with a sequential value from `sim.tag`.

Before implementing any more of the TE dynamics, let's implement the final output event:

```
    5000 late() {
        // print information on each TE, including the fraction of it disabled
        all_tes = sortBy(sim.mutationsOfType(m2), "position");
        all_disabledTEs = sortBy(sim.mutationsOfType(m3), "position");
        genomeCount = size(sim.subpopulations.genomes);
        
        catn("Active TEs:");
        for (te in all_tes)
        {
            cat("   TE at " + te.position + ": ");
            
            active = sim.mutationCounts(NULL, te);
            disabledTE = all_disabledTEs[all_disabledTEs.tag == te.tag];
            
            if (size(disabledTE) == 0)
            {
                disabled = 0;
            }
            else
            {
                disabled = sim.mutationCounts(NULL, disabledTE);
                all_disabledTEs = all_disabledTEs[all_disabledTEs != disabledTE];
            }
            
            total = active + disabled;
            
            cat("frequency " + format("%0.3f", total / genomeCount) + ", ");
            catn(round(active / total * 100) + "% active");
        }
        
        catn("\nCompletely disabled TEs: ");
        for (te in all_disabledTEs)
        {
            freq = sim.mutationFrequencies(NULL, te);
            cat("   TE at " + te.position + ": ");
            catn("frequency " + format("%0.3f", freq));
        }
    }
```

This prints all of the active TEs in the model (sorted by position), with information on their overall frequency in the population and on the fraction of their occurrences that have been disabled by mutations. After that, it prints a list of the completely disabled TEs (sorted as well); frequencies are also given for those, since TEs could conceivably be disabled before fixing. The logic of this code is quite straightforward, so there is no need to belabor it here.

We want our TEs to copy themselves; this occurs during the life of the organism, not during meiosis, so we model it with a `late()` event:

```
late() {
    // make active transposons copy themselves with rate teJumpP
    for (individual in sim.subpopulations.individuals)
    {
       for (genome in individual.genomes)
       {
          tes = genome.mutationsOfType(m2);
          teCount = tes.size();
          jumpCount = teCount ? rpois(1, teCount * teJumpP) else 0;
          
          if (jumpCount)
          {
             jumpTEs = sample(tes, jumpCount);
             
             for (te in jumpTEs)
             {
                // make a new TE mutation
                pos = rdunif(1, 0, L-1);
                jumpTE = genome.addNewDrawnMutation(m2, pos);
                jumpTE.tag = sim.tag;
                sim.tag = sim.tag + 1;
             }
          }
       }
    }
}
```

This loops through the genomes of all individuals in the simulation. For each genome, it gets all of the TEs present, and decides how many (if any) will "jump" according to the probability `teJumpP` for each TE, using a draw from a Poisson distribution. (This is faster than doing a separate random draw for each TE, but is otherwise equivalent.) If any TEs did jump, the ones that jumped are selected at random. Each jump is simulated by creating a new TE at a new, randomly chosen location. The new TEs get new `tag` values assigned sequentially from `sim.tag`, so that their corresponding disabled versions can be looked up. And that is it for jumping; its logic is fairly straightforward since disabled TEs are not involved at all.

Finally, we need to implement the disabling of TEs by random point mutations. Since TEs are simulated here as point mutations themselves, we need to simulate this disabling process ourselves; SLiM's automatic mutation generation will never modify our TEs for us. We model disabling mutations in a `modifyChild()` callback. Its logic is similar to that of the jumping code above, except that when a TE is disabled, a mutation of type `m3` needs to be substituted in place of the existing `m2` mutation that represents the TE. The `m3` mutation corresponding to any given `m2` TE is created just once, and then the same `m3` mutation is looked up and reused every time that same `m2` TE is disabled in another genome. This "uniquing" of the `m3` mutations makes the model much more memory-efficient, and makes the output code much simpler. The main purpose of the `tag` values we have been managing is, in fact, to facilitate this uniquing process. The disabling callback looks like this:

```
modifyChild() {
    // disable transposons with rate teDisableP
    for (genome in child.genomes)
    {
       tes = genome.mutationsOfType(m2);
       teCount = tes.size();
       mutatedCount = teCount ? rpois(1, teCount * teDisableP) else 0;
       
       if (mutatedCount)
       {
          mutatedTEs = sample(tes, mutatedCount);
          
          for (te in mutatedTEs)
          {
             all_disabledTEs = sim.mutationsOfType(m3);
             disabledTE = all_disabledTEs[all_disabledTEs.tag == te.tag];
             
             if (size(disabledTE))
             {
                // use the existing disabled TE mutation
                genome.removeMutations(te);
                genome.addMutations(disabledTE);
                next;
             }
             
             // make a new disabled TE mutation with the right tag
             genome.removeMutations(te);
             disabledTE = genome.addNewDrawnMutation(m3, te.position);
             disabledTE.tag = te.tag;
          }
       }
    }
    
    return T;
}
```

For each genome in the proposed child, we get the TEs contained, and calculate the number that will be disabled using a Poisson draw as before. We select the TEs that actually mutated, and for each, attempt to look up a corresponding `m3` mutation using the `tag` value of the `m2` mutation. If we find one, we substitute that. If not, we create a new `m3` mutation to represent the disabled state, marking it with the TE's `tag` value so we can look it up next time. That's it for the TE disabling code; a bit lengthy, but the logic is simple.

If this model is run, typical output might look like this:

```
Active TEs:
   TE at 1793: frequency 0.011, 100% active
   TE at 2435: frequency 0.208, 100% active
   TE at 3629: frequency 0.002, 100% active
   TE at 6339: frequency 0.208, 94% active
   TE at 7081: frequency 0.020, 100% active
   TE at 7728: frequency 1.000, 79% active
   ...
Completely disabled TEs:
   TE at 24821: frequency 1.000
   TE at 83627: frequency 1.000
   TE at 98286: frequency 1.000
   ...
```

That output shows a mix of TEs at high frequency (perhaps present already in the initial population setup, since not that many generations have elapsed) and TEs at low frequency (which must be copies due to jumping). Some TEs are completely active, whereas others have been partially or fully disabled by mutations. (Once even a single copy of a TE is disabled by mutation, that copy might drift to fixation; the fact that TEs have been completely disabled does not mean that TE-disabling mutations are particularly common.)

Note that this model is never at equilibrium; the number of TEs is likely to grow without bound, since the probability of jumping is greater than the probability of TEs being disabled by mutations. That means that the model runs ever more slowly, since the TE mutations are not allowed to fix. If a model didn't care about disabled TEs at all, it would be much simpler and faster to simply delete TEs from a genome when they are disabled.

Note also that the probabilities of jumping and of being disabled in this recipe are arbitrary and have almost no empirical basis; they just worked well for testing the code. Please do not use these values in any production code of your own.

With that, we have wrapped up this recipe, but obviously there are a great many aspects of the biology of transposons that we haven't covered here:

- Effects of transposons on fitness could be modeled through `fitness()` callbacks, either modifying the fitness effects of other mutations due to the proximity of transposons, or modeling a direct fitness effect for the transposons themselves in their own `fitness()` callback. Alternatively, at the moment of a transposon's jump a genetic effect could be modeled by examining and altering other mutations in the vicinity of the jump destination, to simulate up/down-regulation of those mutations (taking care to make a private copy of any modified mutations first, so that other genomes sharing the same mutations do not receive the same modifications as an unintended side effect).
- Transposons that relocate themselves, rather than copying themselves, could be implemented by adding a call to `genome.removeMutations(te)` in the jump code.
- Attempts by the organism to suppress TEs *en masse*, for example through epigenetic controls such as methylation, could be simulated by converting TEs in a given individual into a suppressed version (perhaps using a new mutation type to represent suppression); such suppression could be temporary, since one could write code to convert suppressed TEs back into active TEs again, too.
- Non-autonomous TEs that can jump only in the presence of a separate enabling gene could easily be modeled simply by checking for the presence of the enabling gene in an individual prior to allowing any TEs in that individual to jump.
- It is not clear exactly what, if anything, restricts the proliferation of TEs in real organisms, but one could certainly model some sort of balancing factor that would limit the proliferation of TEs in this model. The probability of jumping could decrease as the number of active TEs increases (for some unclear reason), or the fitness of organisms could start to decrease sharply as their TE load increases above some bound (with perhaps a bit more biological justification), or whatever other mechanism one wished.
- One of the most interesting aspects of transposons is that they sometimes jump more frequently when an individual is subject to environmental stress; that could be modeled by calculating a jump probability for the TEs in an individual that depends upon that individual's fitness, or upon the mismatch between its phenotype and its environment in some specific trait, if desired.

The point is that although this recipe is fairly rudimentary, many aspects of the evolutionary dynamics of transposons could be easily modeled in SLiM by implementing whatever extensions to this recipe are desired, as outlined above.

13.17 A QTL-based model with two quantitative phenotypic traits and pleiotropy

Sections 13.1 and 13.10 introduced some strategies for modeling quantitative traits in SLiM, where a phenotypic trait's quantitative value is based upon the additive effects of multiple QTLs (quantitative trait loci). Chapter 14 will show more QTL-based models that incorporate continuous space and spatial interactions. All of these quantitative-trait models share the same basic approach: QTL mutations are intrinsically neutral (enforced with a `fitness()` callback), but have an additive effect upon a phenotypic trait value possessed by each individual. Individual fitness is then modeled using some form of fitness function (often Gaussian), based upon the deviation of the individual's phenotype from the optimum phenotype in its environment (determined by a `fitness(NULL)` callback that evaluates each individual). All of these recipes model a single phenotypic trait, however, with the QTL mutations influencing only that one trait. In this section we will look at an extension of the same basic approach, modeling two phenotypic traits. QTL mutations in this model will influence *both* phenotypic traits, pleiotropically, with effect sizes drawn from a multivariate normal distribution (thus allowing the effects on the phenotypic traits to be either independent or correlated). This recipe can be trivially extended to encompass any number of QTL-based phenotypic traits, with any type of pleiotropy. Finally, at the end, we will add in live R-based plotting, as introduced in section 13.11, to plot the adaptive trajectory of the population. You may wish to review sections 13.1, 13.10, and 13.11 before proceeding.

Let's begin with the `initialize()` callback as usual:

```
initialize() {
    initializeMutationRate(1e-7);

    initializeMutationType("m1", 0.5, "f", 0.0);   // neutral
    initializeMutationType("m2", 0.5, "f", 0.0);   // QTLs
    m2.convertToSubstitution = F;
    m2.color = "red";

    // g1 is a neutral region, g2 is a QTL
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElementType("g2", c(m1,m2), c(1.0, 0.1));

    // chromosome of length 100 kb with two QTL regions
    initializeGenomicElement(g1, 0, 39999);
    initializeGenomicElement(g2, 40000, 49999);
    initializeGenomicElement(g1, 50000, 79999);
    initializeGenomicElement(g2, 80000, 89999);
    initializeGenomicElement(g1, 90000, 99999);
    initializeRecombinationRate(1e-8);

    // QTL-related constants used below
    defineConstant("QTL_mu", c(0, 0));
    defineConstant("QTL_cov", 0.25);
    defineConstant("QTL_sigma", matrix(c(1,QTL_cov,QTL_cov,1), nrow=2));
    defineConstant("QTL_optima", c(20, -20));

    catn("\nQTL DFE means: ");
    print(QTL_mu);
    catn("\nQTL DFE variance-covariance matrix: ");
    print(QTL_sigma);
}
```

QTLs will be represented by `m2`; it is declared to be neutral here, so a `fitness(m2)` callback making it neutral will not be needed. In other QTL recipes the selection coefficient of the mutations was used to store the additive effect of each QTL mutation, but we will take a different approach here. The m2 mutations are colored red in SLiMgui, and are not converted to substitutions when they fix, since their phenotypic effect will continue to be important. The chromosome is a mixture of g1 neutral regions and g2 regions that can contain QTL mutations. Finally, we define some QTL-related constants: QTL_mu gives the mean effect of new QTL mutations on the two phenotypes, QTL_cov gives the covariance between the two effects, and QTL_sigma is a variance-covariance matrix derived from QTL_cov that will govern new mutational effects (this matrix is sometimes called an M-matrix). QTL_optima gives the optimal phenotypic values for the two quantitative traits; note that the optima have different signs, but the M-matrix encodes a positive mutational correlation, so adaptation in this model will be contrary to the pleiotropically preferred direction of evolution. Finally, the means and M-matrix are printed; the M-matrix looks like this:

```
QTL DFE variance-covariance matrix:
     [,0] [,1]
[0,]    1 0.25
[1,] 0.25    1
```

Support for matrices was added to Eidos in SLiM 2.6, so the matrix() function and other aspects of working with matrices in Eidos may be new; see the Eidos language manual.

Next we start a new subpopulation:

```
1 late() {
    sim.addSubpop("p1", 500);
}
```

Then we need to draw the effects of new mutations in each generation, which is a bit complex since SLiM doesn't do it for us in this recipe the way it usually does:

```
late() {
    // add effect sizes into new mutation objects
    all_m2 = sim.mutationsOfType(m2);
    new_m2 = all_m2[all_m2.originGeneration == sim.generation];

    if (size(new_m2))
    {
       // draw mutational effects for all new mutations at once
       effects = rmvnorm(size(new_m2), QTL_mu, QTL_sigma);

       // remember all drawn effects, for our final output
       old_effects = sim.getValue("all_effects");
       sim.setValue("all_effects", rbind(old_effects, effects));

       for (i in seqAlong(new_m2))
       {
          e = effects[i,];   // each draw is one row in effects
          mut = new_m2[i];
          mut.setValue("e0", e[0]);
          mut.setValue("e1", e[1]);
       }
    }
}
```

This late() event runs in every generation. It finds new m2 mutations just introduced by SLiM during offspring generation, and patches in QTL effects sizes for them. First, new_m2 is set to the mutations whose originGeneration property is the current generation; these are are new mutations. If there are any, it calls `rmvnorm()` to draw their effect sizes. This function draws from the multivariate normal distribution defined by `QTL_mu` and `QTL_sigma`; we ask it to draw a pair of effects for each new mutation, and it returns a matrix with one row for each mutation and two columns, one for each effect size. We keep a record of all drawn effect sizes in the `"all_effects"` key of the simulation object, for purposes of output. After that, all that remains is to loop through the new mutations and put their drawn effect sizes into their `"e0"` and `"e1"` keys.

Now that mutations have effect sizes assigned to them, we can add code to calculate the phenotypes of individuals as the sum of those additive effects:

```
late() {
    // construct phenotypes from additive effects of QTL mutations
    inds = sim.subpopulations.individuals;

    for (ind in inds)
    {
       muts = ind.genomes.mutationsOfType(m2);

       // we have to special-case when muts is empty
       if (size(muts)) {
          ind.setValue("phenotype0", sum(muts.getValue("e0")));
          ind.setValue("phenotype1", sum(muts.getValue("e1")));
       } else {
          ind.setValue("phenotype0", 0.0);
          ind.setValue("phenotype1", 0.0);
       }
    }
}
```

This event must be *after* the previous `late()` event in the script, so that it runs after mutation effects have been assigned. It loops through the individuals in the subpopulation, and for each individual it gets all of the `m2` mutations possessed in both genomes, adds up their effects, and stores the result as a phenotype. There are only two important differences between this and previous QTL recipes. First, it gets the effects from the `"e0"` and `"e1"` keys of the mutations, rather than from `tag` or `tagF` properties; and second, it stores the phenotypes in `"phenotype0"` and `"phenotype1"` keys on the individuals, rather than in `tag` or `tag` properties. Using tags works well when you have only a single value to store; they are simple to use, and are fast to get and set. Using key-value pairs as in this recipe is a bit more complex, and a bit slower, but more general and extensible; any number of keys can be defined on an object, and so this recipe can be easily extended to any number of phenotypic traits, each influenced by separate mutational effects.

Next, we need those phenotypes to influence the fitness of individuals:

```
fitness(NULL) {
    // phenotype 0 fitness effect, with optimum of QTL_optima[0]
    phenotype = individual.getValue("phenotype0");
    return 1.0 + dnorm(QTL_optima[0] - phenotype, 0.0, 20.0) * 10.0;
}
fitness(NULL) {
    // phenotype 1 fitness effect, with  optimum of QTL_optima[1]
    phenotype = individual.getValue("phenotype1");
    return 1.0 + dnorm(QTL_optima[1] - phenotype, 0.0, 20.0) * 10.0;
}
```

This should be familiar from previous QTL recipes; fitness is drawn from a Gaussian function based on the difference between the individual's phenotype and the optimum. Here we have two separate callbacks, one for each phenotype, for conceptual clarify; these could be combined into a single `fitness(NULL)` callback, of course, combining the fitness effects of the two traits multiplicatively. Furthermore, if one wished the two traits to be subject to a single multivariate Gaussian fitness function, instead of having independent effects on fitness, a `dmvnorm()` function is available in Eidos to facilitate such scenarios, but we shall not do so here. A width of `20.0` is hard-coded here for the fitness functions, but the optima are taken from the constant we defined earlier, and the individual phenotypic values are fetched by key. The `10.0` multiplier makes it so an individual precisely at the phenotypic optimum has a fitness of `10.0` relative to an individual with a phenotype infinitely far from the optimum; strong selection, but not unrealistically so.

All that remains is output and a termination condition. For this model, this is quite complex since we want to look at a bunch of things:

```
1:1000000 late() {
    // output, run every 1000 generations
    if (sim.generation % 1000 != 0)
       return;

    // print final phenotypes versus their optima
    inds = sim.subpopulations.individuals;
    p0_mean = mean(inds.getValue("phenotype0"));
    p1_mean = mean(inds.getValue("phenotype1"));

    catn();
    catn("Generation: " + sim.generation);
    catn("Mean phenotype 0: " + p0_mean + " (" + QTL_optima[0] + ")");
    catn("Mean phenotype 1: " + p1_mean + " (" + QTL_optima[1] + ")");

    // keep running until we get within 10% of both optima
    if ((abs(p0_mean - QTL_optima[0]) > abs(0.1 * QTL_optima[0])) |
       (abs(p1_mean - QTL_optima[1]) > abs(0.1 * QTL_optima[1])))
       return;

    // we are done with the main adaptive walk; print final output

    // get the QTL mutations and their frequencies
    m2muts = sim.mutationsOfType(m2);
    m2freqs = sim.mutationFrequencies(NULL, m2muts);

    // sort those vectors by frequency
    o = order(m2freqs, ascending=F);
    m2muts = m2muts[o];
    m2freqs = m2freqs[o];

    // get the effect sizes
    m2e0 = m2muts.getValue("e0");
    m2e1 = m2muts.getValue("e1");

    // now output a list of the QTL mutations and their effect sizes
    catn("\nQTL mutations (f: e0, e1):");
    for (i in seqAlong(m2muts))
    {
       mut = m2muts[i];
       f = m2freqs[i];
       e0 = m2e0[i];
       e1 = m2e1[i];
       catn(f + ": " + e0 + ", " + e1);
    }
```

```
        // output the covariance between e0 and e1 among the QTLs that fixed
        fixed_m2 = m2muts[m2freqs == 1.0];
        e0 = fixed_m2.getValue("e0");
        e1 = fixed_m2.getValue("e1");
        e0_mean = mean(e0);
        e1_mean = mean(e1);
        cov_e0e1 = sum((e0 - e0_mean) * (e1 - e1_mean)) / (size(e0) - 1);

        catn("\nCovariance of effects among fixed QTLs: " + cov_e0e1);
        catn("\nCovariance of effects specified by the QTL DFE: " + QTL_cov);

        // output the covariance between e0 and e1 across all draws
        effects = sim.getValue("all_effects");
        e0 = effects[,0];
        e1 = effects[,1];
        e0_mean = mean(e0);
        e1_mean = mean(e1);
        cov_e0e1 = sum((e0 - e0_mean) * (e1 - e1_mean)) / (size(e0) - 1);

        catn("\nCovariance of effects across all QTL draws: " + cov_e0e1);

        sim.simulationFinished();
    }
```

This should be fairly self-explanatory, so we won't go through it in any great detail. Every thousand generations it prints a summary of the adaptation so far, like this:

```
Generation: 1000
Mean phenotype 0: 0 (20)
Mean phenotype 1: 0 (-20)

Generation: 2000
Mean phenotype 0: 2.89204 (20)
Mean phenotype 1: -3.42491 (-20)

Generation: 3000
Mean phenotype 0: 2.95127 (20)
Mean phenotype 1: -5.91266 (-20)

...
```

The mean trait value is printed for each phenotypic trait, with the optimum in parentheses; the population didn't manage to adapt at all by generation `1000` (no QTL mutations had arisen without being lost), but by generation `3000` things are moving along better, especially for the second trait. The model continues running until both phenotypic means get within 10% of their optima. That can take a while, since evolution has to run counter to the M-matrix, and since selection gets weaker as the optima are approached. When it gets there, the model produces some final output:

```
...

Generation: 31000
Mean phenotype 0: 21.2388 (20)
Mean phenotype 1: -17.9747 (-20)

Generation: 32000
Mean phenotype 0: 20.7437 (20)
Mean phenotype 1: -18.6298 (-20)
```

```
QTL mutations (f: e0, e1):
1: 2.70148, -0.0621418
1: -0.291556, -1.16253
1: 0.923384, -1.24329
1: -0.431645, 0.170891
1: 1.82426, 0.911538
1: 0.0652766, -1.76526
1: 0.444558, -1.22771
1: 1.62655, -1.33047
1: 1.47864, -0.957393
1: 1.44353, -1.7145
1: 0.496692, -0.441125
1: 1.25745, 1.08043
1: -0.707134, -1.06546
0.801: -0.566786, -0.611955
0.017: -0.308758, -1.02767
0.001: -0.408555, -0.222152

Covariance of effects among fixed QTLs: 0.26061

Covariance of effects specified by the QTL DFE: 0.25

Covariance of effects across all QTL draws: 0.236848
```

After the output of the mean phenotypes, we get a dump of all of the segregating QTL mutations in the population, sorted by frequency. Most of the QTLs have fixed, one is approaching fixation, and two are at very low frequency. Their effect sizes on the two phenotypic traits are shown in the next two columns. Finally, we get a summary of the observed covariance in effects among the QTL mutations that fixed, the requested covariance, and the observed covariance across all effects drawn during the run (including many QTL mutations that were lost). You might expect that the covariance among the fixed QTLs would have to be negative, in order for adaptation to reach the two optima with different signs, but that is not the case; often it is true, but sometimes, as in this run, the optima can be reached even with a positive covariance among the mutational effects.

So we have a two-trait QTL-based adaptive walk model with pleiotropy and correlated mutational effects! As an aside, for advanced users planning to implement QTL models of their own: it is not, in fact, necessary to prevent the QTL mutations from fixing by setting `convertToSubstitution=F`. Instead, you can allow them to fix, and then add in the effects of the `Substitution` objects on the calculated phenotypes. This will be faster, if implemented carefully (tip: add newly fixed substitutions to an accumulator total), since the SLiM core won't get bogged down managing the bookkeeping on an ever-growing set of QTL mutations.

Now let's add a little extra code to plot the trajectory of the adaptive walk in SLiMgui, using the live R plotting technique of section 13.11. First let's open a PDF-based plot window in SLiMgui:

```
1 late() {
    sim.setValue("history", matrix(c(0.0, 0.0), nrow=1));
    defineConstant("pdfPath", writeTempFile("plot_", ".pdf", ""));

    // If we're running in SLiMgui, open a plot window
    if (exists("slimgui"))
      slimgui.openDocument(pdfPath);
}
```

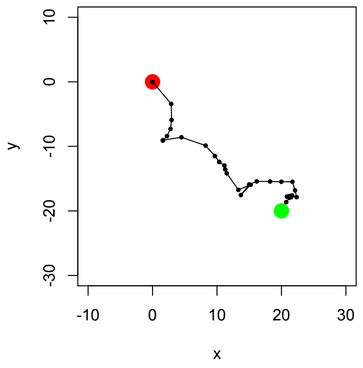
This starts a history of the population's adaptive walk in a new key named `"history"` on the simulation object. It also makes a temporary PDF file with `writeTempFile()`, and tells SLiMgui to open that file; see section 13.11 for details.

Now we just need to update that plot with periodic callouts to R. To do so, insert the following code inside the `1:1000000` final output event, immediately above the comment "keep running until we get within 10% of both optima":

```
// update our plot
history = sim.getValue("history");
history = rbind(history, c(p0_mean, p1_mean));
sim.setValue("history", history);

rstr = paste(c('{',
   'x <- c(' + paste(history[,0], sep=", ") + ')',
   'y <- c(' + paste(history[,1], sep=", ") + ')',
   'quartz(width=4, height=4, type="pdf", file="' + pdfPath + '")',
   'par(mar=c(4.0, 4.0, 1.5, 1.5))',
   'plot(x=c(-10,30), y=c(-30,10), type="n", xlab="x", ylab="y")',
   'points(x=0,y=0,col="red", pch=19, cex=2)',
   'points(x=20,y=-20,col="green", pch=19, cex=2)',
   'points(x=x, y=y, col="black", pch=19, cex=0.5)',
   'lines(x=x, y=y)',
   'dev.off()',
   '}'), sep="\n");

scriptPath = writeTempFile("plot_", ".R", rstr);
system("/usr/local/bin/Rscript", args=scriptPath);
```

This updates the `"history"` key with the latest data, and then generates a string contain R plotting code and sends that code to R to run. The R code is based on Mac OS X, using the `quartz()` function of R to open a new plotting device. Again, see section 13.11 for details on this technique).

When run in SLiMgui, a plot window will open and update every 1000 generations to show the adaptive trajectory thus far. For the same run of the model as shown in the output above, the resulting plot looks like this (the walk begins at the red disc, and the green disc is the optimum):



This sort of live visualization of model dynamics can be extremely help for both model design and graphical debugging, and is quite simple to set up, as we have seen here.

In closing, it is perhaps emphasizing once more that although this recipe models two phenotypic traits, it is designed to be extensible. It uses key-value pairs set on the mutations and individuals to track the QTL mutational effects and phenotypic trait values; any number of such key-value pairs can be maintained. The `rmvnorm()` function can also draw from a multivariate normal distribution of any dimensionality, with any (positive-definite) M-matrix. This design is thus quite open-ended.

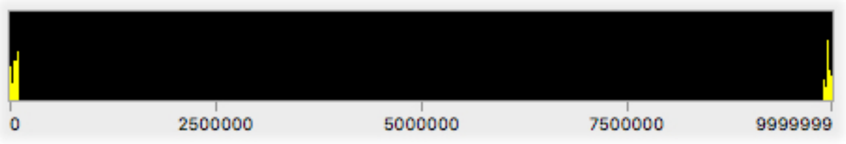
13.18 Modeling opposite ends of a chromosome

This recipe is not about how to model something complicated; instead, it is intended to illuminate something conceptual about using SLiM in certain situations.

Consider the following recipe:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeGenomicElement(g1, 9900000, 9999999);
    initializeRecombinationRate(1.5e-7);
}
1 { sim.addSubpop("p1", 500); }
200000 late() { sim.outputFixedMutations(); }
```

This is a simple neutral model of a chromosome of length `L==1e7` bases. The only unusual thing about it is that we are actually only modeling the two ends of the chromosome; we have defined a genomic element spanning the first `1e5` bases, and another spanning the last `1e5` bases, and the intervening region, which is 98% of the length of the chromosome, is not modeled. In SLiMgui, the model looks like this after a little while:



This is perfectly fine; all that it means is that SLiM will not automatically generate mutations within the region that is not covered by any genomic element, and so that central region remains empty. The region does not *have* to remain empty; it would be legal to call `addNewMutation()` to create a new mutation within that region, and SLiM would then track that added mutation normally. The only effect that genomic elements have, in SLiM, is in causing the automatic generation of new mutations by the SLiM core. But let's keep the model as it is, and ask: what is the behavior of the two end regions, with respect to recombination between them? Do they assort independently, as if they were separate chromosomes, since they are separated by a rather long stretch of chromosome? Or if not, then what is the effective recombination rate between them?

First of all, let's make sure we understand exactly what "recombination rate" really means in SLiM. As section 21.1 states, the recombination rate is the probability that a crossover will occur between two adjacent bases. This is binomial; conceptually, a coin is flipped, and the coin lands "heads" (crossover) with probability *p*, and "tails" (no crossover) with probability 1-*p*, and that is done at every position between adjacent bases along the whole chromosome. There are `L-1` positions between bases in a chromosome of length `L`. In this model, `2e5-2` of them occur between the bases spanned by the two genomic elements, and the remainder, `9800002`, occur between those two regions. Those are the positions we're interested in, and at each position a crossover occurs with probability `r=1.5e-7`.

To get the probability that the two genomic elements will assort apart, rather than together, we cannot simply multiply the number of positions (`9800002`) by the probability per position (`1.5e-7`), of course; that would give us `1.47`, a nonsensical result that isn't even a valid probability. Instead, we need to observe that the key question is actually whether the number of crossovers that occur between the two regions is *even* or *odd*. An even number of crossovers will cancel out; we will cross over and then cross back, perhaps repeatedly, with no net effect. The two genomic elements will then assort together. An odd number of crossovers, on the other hand, will result in all but one crossover canceling out, and one crossover will remain; the two genomic elements will then assort apart.

So the question then becomes: for a binomial draw with `9800002` trials and a probability per trial of `1.5e-7`, what is the probability that the result of the draw will be odd? There is, of course, established mathematical theory on this point, but let's answer the question through simulation. In an Eidos console, such as the one we can open inside SLiMgui, we can do a large number of draws from that binomial distribution:

```
> draws = rbinom(1e8, 9800002, 1.5e-7)
```

That will take a moment, and then we have `1e8` draws from the requisite binomial distribution. Next let's ask what fraction of them is odd:

```
> sum(draws % 2 == 1) / 1e8
0.473642
```

So, the two genomic elements will assort apart about 47.4% of the time, and the remaining time will assort together.

So now suppose we want to construct a SLiM model that just elides that central region (since we weren't using it anyway) and places the two chromosome ends immediately next to each other. There is no particular obstacle to doing this, except that we need to know what recombination rate to use for the join point between the two halves – which we have just figured out. So we could now rewrite our model as:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeGenomicElement(g1, 100000, 199999);

    rates = c(1.5e-7, 0.473642, 1.5e-7);
    ends = c(99999, 100000, 199999);
    initializeRecombinationRate(rates, ends);
}
1 { sim.addSubpop("p1", 500); }
200000 late() { sim.outputFixedMutations(); }
```

This model ought to behave identically to the previous model, and ought to be somewhat more efficient, too (although the difference may not be large enough to be noticeable). This is because when running the first model SLiM would potentially be generating two or more breakpoints between the two ends, and then resolving whether there were an even or odd number as it ran, whereas when running the second model SLiM either generates zero breakpoints or one breakpoint, with the correct calculated probability.

As turns out, we could get the same probability by using the rate-rescaling formula of section 5.5, since what we are effectively doing is rescaling a region of length `9800002` down to a length of `1` (length in terms of potential recombination positions, that is). That formula, executed in the Eidos console, gives us:

```
> 0.5*(1-(1-2*1.5e-7)^9800002)
0.473567
```

Which is very close to the number we got before (which, remember, was inexact since it came from simulation). So that's pleasing.

The point of this recipe, then, is twofold. One point is to provide another angle of view on the rate-rescaling formula of section 5.5, to illustrate that it applies in situations other than the rescaling of an entire model. The second, more important, point is to illustrate once again that the recombination rate as specified by SLiM is the probability of a crossover occurring between two adjacent bases, and the consequences that that has for reasoning about how recombination works on larger scales.

This is as good a place as any for a digression that I think this manual ought to contain somewhere: how SLiM actually generates recombination breakpoint positions under the hood. This is worth demystifying because for models that use very high recombination rates the subtleties of this process can be important. Mostly, though, this digression is just for those who are curious, and beginning users of SLiM should feel free to skip it.

Overall, SLiM does this in several steps: (1) it decides upon the number of breakpoints it will generate, (2) it chooses the location for each breakpoint based upon a weighted uniform draw along the chromosome (where the weights are equal to the recombination rates for each individual base, as defined by the recombination map), and then (3) it sorts and uniques the list of breakpoints to provide a final list. The uniquing of the list means that there is, at most, one crossover (i.e., breakpoint) between any two base positions; this is biologically realistic, and also computationally simpler.

So the big question is: how to decide upon the number of breakpoints to generate? One way would be to start from the fact that between each pair of bases the question is one of a binomial draw, with a single trial of probability equal to the recombination rate (by SLiM's definition). One could do one such draw per pair of bases, add up the results, and that's the number of crossovers that occurred. The immediate problem with that approach is simply that it is immensely computationally expensive, and if the user has supplied a complex recombination map with different rates at every position it can't be reduced to a single binomial draw with a larger number of trials.

So perhaps we might wish to model recombination as a Poisson process instead, leveraging the fact that Poisson draws can be added together: Poisson(λ_1) + Poisson(λ_2) = Poisson($\lambda_1 + \lambda_2$). If two adjacent base positions have a probability of a crossover between them of λ, then the mean of the binomial draw can be used as the mean of a Poisson draw instead (the Poisson distribution being well-known as a viable approximation for the binomial distribution with small λ and largish n). Then we can add up the λ values across the chromosome and get the number of recombination events with a single Poisson draw that uses that total λ value. And indeed, this is precisely what SLiM 2.x and earlier did.

Unfortunately, as SLiM users started moving towards new areas of modeling in SLiM such as multiple chromosomes, it became clear that there was a problem with this approach. When modeling multiple chromosomes, you want, intuitively, to connect them together in SLiM with a recombination rate of `0.5` to represent perfect independence of assortment. Unfortunately, this value is large enough that the Poisson approximation of the binomial distribution breaks down. The Poisson draw can not only be `0` or `1` (as with the binomial), but also larger values, and with a rate of `0.5` this happens often enough to matter. In SLiM's case, if the Poisson draw indicated that (for example) two crossovers occurred, their positions would be sorted and uniqued (to prevent multiple crossovers at the same exact location, as described above), resulting in just one crossover where the Poisson draw had specified two. The net effect of this would be that the probability of a crossover at the given location would be somewhat lower than desired – about `0.39`, in fact, rather than `0.5`. (It is lower than `0.5` because more than half of the Poisson draws for λ=`0.5` will be zero, compensating for the fact that some of the draws are greater than one and making the mean of the Poisson distribution come out to `0.5`).

So at first blush it looks like we can't use a binomial draw (too complicated in the case of complex recombination maps) and we can't use a Poisson draw (inaccurate with large recombination rates such as `0.5`). What to do?

The solution we arrived at, thanks to Peter Ralph, is to reparameterize the Poisson draws that we're doing. If the user has requested a recombination rate of *p* (probability of crossover between two adjacent bases), but we want to use a Poisson draw and have it generate a crossover, after sorting and uniquing, with probability *p*, then we can transform the requested *p* into a reparameterized value λ such that Prob[(Poisson(λ) > 0) = *p*]. The formula for this reparameterization is:

$$\lambda = -\,log(1 - p)$$

With this reparameterization, we end up with the correct probability of crossover after using a Poisson(λ) draw, accounting for SLiM's sorting and uniquing of the breakpoint vector. This means that we can add up the λ values for each region along a whole chromosome, even with a complex recombination map, and draw a preliminary number of crossovers from a Poisson distribution with the total λ, and then after we select locations with the usual weighted uniform draws, and sort and unique them, the probability of crossover at every specific site will be as the user requested. It will work even when some positions have a rate of `0.5`; and even though the Poisson distribution is only an approximate estimation for the binomial distribution, this solution is in fact exact, since it is based upon the probability that the Poisson draw for a specific position is greater than zero, not upon the mean of the Poisson distribution.

If that was all gibberish, never mind. The point is that, as of SLiM 3, recombination rates should be accurate (within numerical precision limits) even for large recombination rates like `0.5`, with no sacrifice in speed.

13.19 Biased gene conversion

SLiM intrinsically supports gene conversion (see section 6.1.3), but it does not intrinsically support *biased* gene conversion. This is unsurprising, since SLiM has no intrinsic support for modeling nucleotides – biased gene conversion has to do with a bias in the gene conversion process based upon the specific nucleotides in or near the gene conversion tract (Galtier et al. 2001; Ratnakumar et al. 2010). Nevertheless, it is possible to wedge a concept of biased gene conversion into SLiM, and in this section we will do so in two very different recipes. The first recipe will be a nucleotide-based model, using the techniques introduced in section 13.12 to model nucleotides in SLiM. The second recipe will not be nucleotide-based, even those biased gene conversion is a nucleotide-based phenomenon; it will model it as a more abstract process. Which approach is better will depend upon your purposes. Indeed, we do not necessarily recommend either approach; a different software package that is more specifically designed to model nucleotide evolution might be more appropriate for this task. But for those who wish to do it in SLiM, we will look at how it might be done.

Our first model, then, is nucleotide-based. See section 13.12 for an introduction to how nucleotide-based models can be simulated in SLiM; we will follow a somewhat different approach here but the underlying idea is the same. We will discuss the model in parts, but will not build it step by step. We will begin with the `initialize()` callback:

```
initialize() {
    defineConstant("L", 1e4);      // number of loci

    // mutation type for each nucleotide, all neutral
    mtA = initializeMutationType(0, 0.5, "f", 0.0);
    mtT = initializeMutationType(1, 0.5, "f", 0.0);
    mtG = initializeMutationType(2, 0.5, "f", 0.0);
    mtC = initializeMutationType(3, 0.5, "f", 0.0);
    mt = c(mtA, mtT, mtG, mtC);

    mtA.setValue("nucleotide", "A");
    mtT.setValue("nucleotide", "T");
    mtG.setValue("nucleotide", "G");
    mtC.setValue("nucleotide", "C");
    c(mtA,mtT).color = "blue";
    c(mtG,mtC).color = "red";

    // We do not want mutations to stack or fix
    mt.mutationStackPolicy = "l";
    mt.mutationStackGroup = -1;
    mt.convertToSubstitution = F;

    // chromosome of nucleotides, with gene conversion
    initializeGenomicElementType("g1", mt, c(1,1,1,1));
    initializeGenomicElement(g1, 0, L-1);
    initializeMutationRate(1e-6);   // includes 25% identity mutations
    initializeRecombinationRate(1e-6);
    initializeGeneConversion(0.5, 100);
}
```

This is a simpler setup than in section 13.12; we have one mutation type for each nucleotide type, rather than one mutation type per nucleotide type *per base position*. This simplicity is possible here because this will be a pure neutral model; the different mutation types were used in section 13.12 to allow each nucleotide at each position to have an independent fitness effect, but since this model will be neutral that complexity is not necessary. It ought to be possible to generalize this recipe to the non-neutral model of section 13.12, but we will not explore that here. As in section 13.12, we use stacking policy to prevent mutations from stacking or fixing. We model a chromosome `1e4` bases long, and we turn on gene conversion for 50% of all recombination events, with a mean conversion tract length of `100`.

Next we define a utility function:

```
function (f)gcContent(void)
{
    nucs = sim.mutations.mutationType.getValue("nucleotide");
    counts = sim.mutationCounts(NULL);
    totalA = sum(counts[nucs == "A"]);
    totalT = sum(counts[nucs == "T"]);
    totalG = sum(counts[nucs == "G"]);
    totalC = sum(counts[nucs == "C"]);
    total = totalA + totalT + totalG + totalC;
    return (totalC + totalG)*100/total;
}
```

This gets the nucleotides used by all mutations, and count information for all mutations, and uses that information to calculate the percent GC content across the genome. We will use this later to print status updates as the model runs.

Next we set up the initial population:

```
1 late() {
    sim.addSubpop("p1", 1000);
    
    // The initial population is fixed for a random wild-type
    // nucleotide at each locus in the chromosome
    mutTypes = sample(g1.mutationTypes, L, replace=T);
    p1.genomes.addNewDrawnMutation(mutTypes, 0:(L-1));
    
    catn("Initial GC content: " + gcContent());
}
```

We make `1000` individuals, set up random wild-type nucleotides in their genomes (the same nucleotide sequence in every genome, initially), and call our `gcContent()` utility function to print the initial GC content.

Next comes the heart of the model, a `recombination()` callback that implements biased gene conversion based upon the nucleotide sequence:

```
recombination() {
    if (size(gcStarts) != 1)
       return F; // no change unless a gene conversion
    if (size(breakpoints) > 0)
       return F; // no change if any recombination
    
    // We have a gene conversion event; we will accept it if it
    // increases the GC content of the tract in question
    gcMuts1 = genome1.mutations;
    gcMuts1 = gcMuts1[gcMuts1.position >= gcStarts];
    gcMuts1 = gcMuts1[gcMuts1.position < gcEnds];
    gcNucs1 = gcMuts1.mutationType.getValue("nucleotide");
    gcGC1 = sum((gcNucs1 == "G") | (gcNucs1 == "C")) / size(gcNucs1);
    
    gcMuts2 = genome2.mutations;
    gcMuts2 = gcMuts2[gcMuts2.position >= gcStarts];
    gcMuts2 = gcMuts2[gcMuts2.position < gcEnds];
    gcNucs2 = gcMuts2.mutationType.getValue("nucleotide");
    gcGC2 = sum((gcNucs2 == "G") | (gcNucs2 == "C")) / size(gcNucs2);
    
    if (gcGC2 > gcGC1)
       return F; // no change if we like the new tract
    
    // reject the new tract
    gcStarts = integer(0);
    gcEnds = integer(0);
    return T;
}
```

First we check that we have been called with recombination breakpoints representing a single gene conversion event with no other recombination; the code could be made more general, but we will leave that as an exercise for the reader. Given that situation, we get the nucleotides present in the proposed gene conversion tract, from both genomes, and evaluate their GC content. If the GC content of the tract that would be copied by gene conversion is greater than the GC content of the tract that would be overwritten, we allow the proposed gene conversion event to proceed, by returning F to SLiM. Otherwise, we reject the proposed tract, causing that gene conversion event not to occur. (See section 22.5 for background on how `recombination()`

callbacks work and what their return values mean.) Note that this is probably a ridiculously simplified model of how gene conversion actually works; it doesn't even have any sort of probabilistic component, but rather *always* accepts conversions that will increase GC content and *always* rejects others. Again, a more sophisticated model is left as an exercise for the reader; but the code here should illustrate the skeleton of how such a sophisticated model would be approached.

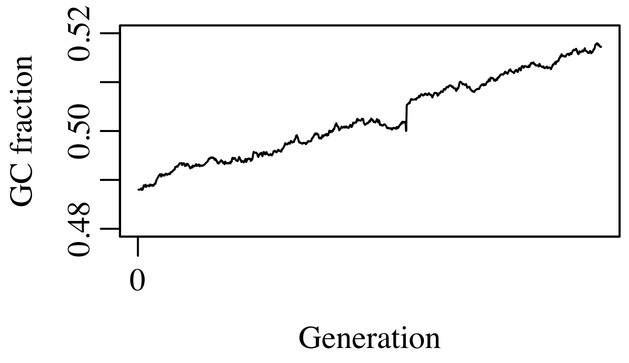
Finally, we output the GC content of the population every thousand generations as the model runs:

```
1:1000000 late() {
    if (sim.generation % 1000 == 0)
       catn(sim.generation + " GC content: " + gcContent());
}
```

This model gives us output like this:

```
Initial GC content: 48.8
1000 GC content: 48.8026
2000 GC content: 48.8009
3000 GC content: 48.803
...
```

The accumulation of increased GC content in this model is a slow affair, but if we run to generation `1000000` and plot the result, we can see that progress is steady:



Of course the rate will depend upon the mutation rate, gene conversion rate, tract length, and other variables; the slow pace here is not inherent to the model, just a consequence of the chosen parameters.

That recipe simulated actual nucleotide sequences, with mutations explicitly changing the sequence in a given genome; at the end of a model run we could print out the nucleotide sequences of all individuals, in FASTA format, perhaps. The next recipe is very different; we will not model nucleotides at all. Instead, we will model a chromosome that is assumed to be an even mix of AT and GC initially (50% GC content, in other words), but we won't try to keep track of which initial locations are AT and which are GC; we have no sequence information at all. We then model two types of mutations on that background: GC to AT, and AT to GC. By counting these mutations, we can know whether a given tract is GC-rich or GC-poor, and we can assess the overall GC content of a genome. Avoiding explicit modeling of nucleotides will make this recipe much simpler and faster than the previous recipe. Again, let's look at this model one block at a time, starting with `initialize()`:

```
initialize() {
    defineConstant("L", 1e5);      // number of loci

    mtAT = initializeMutationType(0, 0.5, "f", 0.0);
    mtAT.color = "blue";
    mtAT.tag = -1;

    mtGC = initializeMutationType(1, 0.5, "f", 0.0);
    mtGC.color = "red";
    mtGC.tag = 1;

    // chromosome of length L, with gene conversion
    initializeGenomicElementType("g1", c(mtAT, mtGC), c(1,1));
    initializeGenomicElement(g1, 0, L-1);
    initializeMutationRate(1e-6);
    initializeRecombinationRate(1e-6);
    initializeGeneConversion(0.5, 100);
}
```

We'll model a chromosome of length `1e5` this time, since this model is faster. We set up the GC-to-AT and AT-to-GC mutation types, give them different colors in SLiMgui, and give them `tag` values of `-1` and `+1` respectively; we will use those `tag` values to easily total up the effect of a vector of mutations on GC content. We use the same mutation rate, recombination rate, and gene conversion properties as in the previous model. Then we set up an initial subpopulation:

```
1 late() {
    sim.addSubpop("p1", 1000);
}
```

And then we introduce a `recombination()` callback that implements the biased gene conversion:

```
recombination() {
    if (size(gcStarts) != 1)
       return F; // no change unless a gene conversion
    if (size(breakpoints) > 0)
       return F; // no change if any recombination

    // We have a single gene conversion event
    gcMuts = genome2.mutations;
    gcMuts = gcMuts[gcMuts.position >= gcStarts];
    gcMuts = gcMuts[gcMuts.position < gcEnds];
    gcGC = sum(gcMuts.mutationType.tag);
    take = (gcGC > 0);

    if (take)
       return F; // no change if we like the new tract

    // reject
    gcStarts = integer(0);
    gcEnds = integer(0);
    return T;
}
```

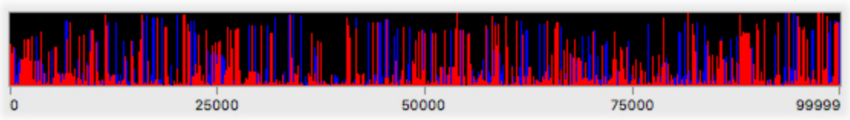
As in the first recipe, this callback runs only is a single gene conversion event with no recombination is being proposed, for simplicity. In that case, we total up the GC-influencing mutations in the proposed gene conversion tract, and if their net effect is to increase GC content we accept the proposed gene conversion event, otherwise we reject it. (Note that this code does not compare the tracts from the two genomes, so its criterion is a bit different from that of the first recipe, but it would be easy to make it match; we're just exploring possibilities here.)

Finally, we have a periodic output event:

```
1:10000000 late() {
    if (sim.generation % 1000 == 0)
      catn(sim.generation + " GC sum: " +
        sum(sim.substitutions.mutationType.tag));
}
```

Since we can tot up the effect of all mutations on GC content very easily, we don't use a utility function here. Note that this code just totals up the substitutions; we don't bother assessing the mean GC content across all genomes. The first recipe didn't use substitutions, since nucleotide-based models generally don't convert fixed mutations to substitutions (because a new mutation that introduces a different nucleotide could always occur).

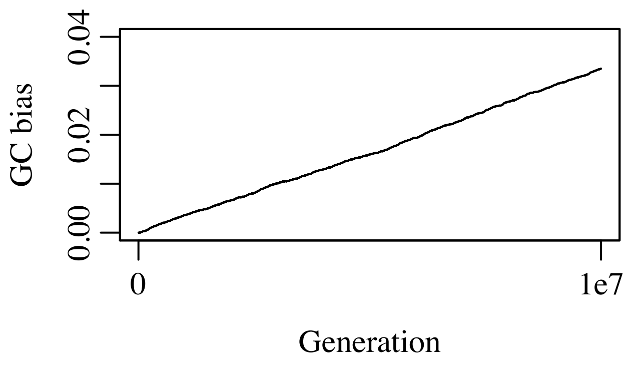
When running in SLiMgui, we can see all of the AT-to-GC (red) and GC-to-AT (blue) mutations circulating in the population:



Since this model, like the previous recipe, is neutral, we can have large numbers of these mutations segregating in the population without it getting too slow. As it runs, this model will produce output like:

```
1000 GC sum: 0
2000 GC sum: -1
3000 GC sum: 0
4000 GC sum: 8
...
```

If plotted, this shows an even steadier increase:



The smoother trajectory here, compared to the previous recipe, may in part be a result of the larger population size. This plot also spans a generation range ten times that of the previous recipe, which smooths the plot out. Finally, there may be some way in which the details of the model, particularly the different criterion used in the `recombination()` callback, produces a smoother increase.

Again, which of these models is best will depend upon the application, and it may be that neither model is particularly ideal, since SLiM is not really designed to simulate nucleotides. However, the output from both models shows clear evidence of biased gene conversion; if a simple model of that process is all that it needed, to simulate its effects upon some other evolutionary process, this level of sophistication may suffice. The second model, in particular, provides relatively low overhead in a SLiM model of biased gene conversion by "thinking outside the box" and modeling the effects of the process – the tendency to accept some gene conversion events and reject others, based upon the mutations present in the gene conversion tract – without explicitly modeling the nucleotides involved. If it is the effects of the process that are important, rather than the specific nucleotide sequences generated, that level of realism may suffice, with considerable savings in computation time.

14. Continuous-space models and interactions

This chapter introduces two new features added in SLiM 2.3: continuous space, and the `InteractionType` class. These two features will be treated together in this chapter, since many of the uses of `InteractionType` involve modeling spatial interactions, but in fact each feature may be used independently of the other. Note that these are advanced, optional features.

Continuous-space support in SLiM is enabled by supplying a `dimensionality` parameter to the `initializeSLiMOptions()` call during model initialization. This parameter may be `"x"`, `"xy"`, or `"xyz"`; these set up SLiM to support 1D, 2D, or 3D continuous space, respectively, within each subpopulation using the coordinate axes specified. (Setting up spaces using different coordinate axes than these, such as 2D space using *y* and *z*, is not presently supported.) The corresponding `x`, `y`, and `z` properties of `Individual` will then be interpreted by SLiM as spatial coordinates, rather than simply as type `float` tag values. Model code can then set the positions of individuals as desired; this is typically done in a `modifyChild()` callback, so that the positions of new offspring are immediately set, but it can also be done at any other point in the generation cycle. Individual positions can also be used by model code in any way desired; for example, spatially continuous variation in selection could be implemented in a `fitness()` callback by computing an environmental value at the spatial location of the focal individual, and then comparing the individual's phenotype to that environmental value (see section 14.9). When continuous space is enabled, SLiMgui will display subpopulations graphically using the spatial positions of individuals.

Interactions between individuals can be implemented in pure Eidos, as seen previously in the frequency-dependent model of section 9.4.1 and the green-beard model of section 9.4.4. This can be cumbersome, however, since all of the interaction mechanics must be written by the user in Eidos, which – as an interpreted language – is not nearly as fast as the C++ in which the SLiM engine is written. The `InteractionType` class provides a solution to this problem, by providing built-in support for fast interaction evaluation while still allowing scripted customization of the interactions through a new type of callback, the `interaction()` callback. `InteractionType` can be used to model non-spatial interactions, as we will see in section 14.6; but it is particularly well-suited to modeling interactions in continuous space, since it is able to translate distances into interaction strengths automatically using any of several different "spatial kernels" (Gaussian, negative exponential, etc.). In addition, `InteractionType` is optimized for spatial searches (such as nearest-neighbor searches) through the use of a data structure called a "k-d tree". Together, these features allow complex spatial interactions to be implemented in just a few lines of Eidos code, with performance that can be orders of magnitude better than would otherwise be possible.

When continuous space is enabled in a model, the `Subpopulation` class now contains several features to support that functionality. First, `Subpopulation` is now aware of its spatial boundaries (the spatial coordinates of the edges of the subpopulation). Second, it can help to enforce those boundaries through various boundary conditions. Third, it now supports "landscape maps", grid-based maps that define the values of particular environmental variables across the spatial extent of the subpopulation. Landscape maps allow simulations to incorporate spatial variation in properties such as elevation or temperature – any variable relevant to the model's dynamics.

With that introduction, let's delve into some recipes that exemplify these new features.

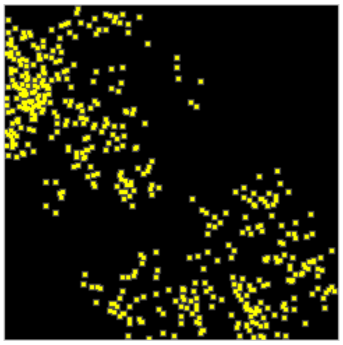
14.1 A simple 2D continuous-space model

In this recipe we will explore a very simple model utilizing continuous space. In this model, individuals will live on a two-dimensional landscape. Individuals will not interact spatially in this model; that will be introduced in section 14.2. The model:

```
initialize() {
    initializeSLiMOptions(dimensionality="xy");
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 late() {
    sim.addSubpop("p1", 500);

    // initial positions are random in ([0,1], [0,1])
    p1.individuals.x = runif(p1.individualCount);
    p1.individuals.y = runif(p1.individualCount);
}
modifyChild() {
    // draw a child position near the first parent, within bounds
    do child.x = parent1.x + rnorm(1, 0, 0.02);
    while ((child.x < 0.0) | (child.x > 1.0));

    do child.y = parent1.y + rnorm(1, 0, 0.02);
    while ((child.y < 0.0) | (child.y > 1.0));

    return T;
}
2000 late() { sim.outputFixedMutations(); }
```

There are only a few new things about this model. First of all, continuous 2-D space is enabled in the model with the call to `initializeSLiMOptions()`. Second, when the subpopulation is created in the `1 late()` event initial positions for all individuals are generated using `runif()`. Note that by default the spatial extent of the subpopulation spans the interval [0,1] in *x* and *y*, so the default `min` and `max` values for `runif()` suffice. Third, a `modifyChild()` callback generates a spatial position for the offspring individual. In this recipe, the offspring position is based upon the position of the first (i.e. maternal) parent, as given by `parent1.x` and `parent1.y`, with random deviations drawn from a normal distribution using `rnorm()`. The new positions could fall outside of the subpopulation's boundaries, so they are redrawn until they fall inside using `while` loops.

When run in SLiMgui, a typical snapshot of this model looks like this:



Here, SLiMgui is displaying each individual at its corresponding spatial position, as a small square (colored according to fitness, as usual). Notably, spatial structure has emerged already in this simple model, because of the way that child positions are based upon maternal positions; this tends to encourage spatial clustering. Since spatial position is of no consequence in the model, however, this makes no difference to the evolutionary dynamics observed.

14.2 Spatial competition

The recipe in the previous section set up spatiality but did not use it. In this section we will extend that recipe to include spatial competition between individuals. The strength of competition between two individuals will depend upon the spatial distance between them, falling off with increasing distance according to a Gaussian kernel with a characteristic width. This could represent, for example, competitive interference due to overlap in foraging areas. The recipe:

```
initialize() {
    initializeSLiMOptions(dimensionality="xy");
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);

    // Set up an interaction for spatial competition
    initializeInteractionType(1, "xy", reciprocal=T, maxDistance=0.3);
    i1.setInteractionFunction("n", 3.0, 0.1);
}
1 late() {
    sim.addSubpop("p1", 500);

    // initial positions are random in ([0,1], [0,1])
    p1.individuals.x = runif(p1.individualCount);
    p1.individuals.y = runif(p1.individualCount);
}
1: late() {
    // evaluate interactions before fitness calculations
    i1.evaluate();
}
fitness(NULL) {
    // spatial competition
    totalStrength = i1.totalOfNeighborStrengths(individual);
    return 1.1 - totalStrength / p1.individualCount;
}
modifyChild() {
    // draw a child position near the first parent, within bounds
    do child.x = parent1.x + rnorm(1, 0, 0.02);
    while ((child.x < 0.0) | (child.x > 1.0));

    do child.y = parent1.y + rnorm(1, 0, 0.02);
    while ((child.y < 0.0) | (child.y > 1.0));

    return T;
}
2000 late() { sim.outputFixedMutations(); }
```

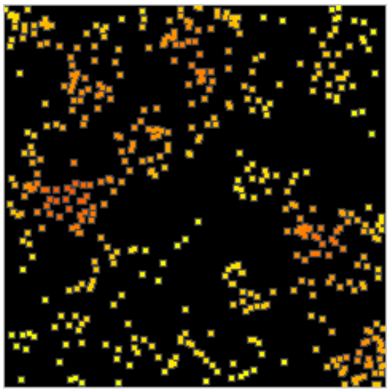
Here we have added a few new elements. First of all, a call to `initializeInteractionType()` creates a new interaction type with identifier `1`, which is therefore referred to as `i1`, in much the same way that mutation types, genomic element types, and subpopulations are numbered and named in SLiM. This call also defines the interaction type as using both the *x* and *y* coordinates of the model, and sets the maximum range for the interaction as `0.3`; beyond that limit interaction strengths are always assumed to be zero, allowing better performance. The interaction is also configured with `reciprocal=T`; this guarantees that the interaction strength exerted upon A by B is equal to the interaction strength exerted upon B by A, allowing computational optimizations. Interactions are non-reciprocal by default, so that bugs are not inadvertently introduced by an implicit assumption of reciprocality; but in practice most interactions are reciprocal and should be specified as such for maximal performance.

Second, a call to `setInteractionFunction()` tells `i1` that it should convert spatial distances into interaction strengths using a Gaussian function (represented by `"n"` for “normal”, to avoid confusion with the `"g"` for “gamma” used elsewhere in SLiM). This Gaussian function is scaled to have a maximum value of `3.0` and a standard deviation of `0.1`, representing fairly local interactions. It can now be seen how the maximum distance set for `i1` was chosen; it is three times the standard deviation of the interaction kernel. Interaction strengths beyond that distance would be extremely small anyway, and are thus neglected by this model for efficiency.

Next, interaction type `i1` needs to actually be used. A precondition for this is that `i1` be “evaluated” in each generation. This is done in the `1: late()` event, with a call to its `evaluate()` method. This takes a snapshot of the model’s spatial state at that moment in time, and `i1` will then calculate all interactions based upon that snapshot. This is necessary because under the hood, `InteractionType` performs a lot of time-consuming analysis to set up spatial data structures representing the state of the model, allowing it to respond quickly to spatial queries. It does that analysis just once, at the point of evaluation, and the results are cached and used for all queries until the interaction is evaluated again. (In fact, this is not quite accurate; `interaction()` callbacks may be called in a deferred fashion, as discussed when we introduce `interaction()` callbacks.)

Having evaluated `i1` in the `late()` event, just before fitness calculation in the generation cycle, the model then uses `i1` in a global `fitness()` callback to calculate fitness values that represent the effects of spatial competition. The call to `totalOfNeighborStrengths()` totals up the interaction strengths between `individual` (the focal individual) and all other interacting individuals in its subpopulation. These interaction strengths, as we saw above, were configured to be calculated using a particular Gaussian kernel, and a maximum distance of `0.3` was chosen. Those settings are now used to find the interaction strength between `individual` and every other individual, and the sum of those strengths is returned. The `fitness()` callback divides that total by the number of individuals in the subpopulation to get a mean interaction strength, and subtracts that mean value from `1.1` to get a fitness value. Those details are fairly arbitrary; the overall intent, however, is that the stronger the competition felt by an individual, the lower the individual’s fitness.

If we run this model in SLiMgui, it looks markedly different from the previous model:



Perhaps the most obvious difference is that individuals are no longer all yellow (which indicated neutrality). Now, individuals in relatively tight spatial clusters are orange or even red, indicating they have fitness values below `1.0` due to the effects of competition. Those individuals will be less likely to reproduce, whereas the individuals enjoying a lack of competition in isolated areas will be more likely to reproduce. That leads to the other obvious difference: the space is more completely and uniformly occupied. This model uses the same offspring positioning algorithm as the previous recipe, which promotes spatial clustering; however, excessive clustering is now opposed by the effects of competition, producing that more uniform distribution.

14.3 Boundaries and boundary conditions

Here we will pause to examine the question of boundaries and boundary conditions in spatial models. When a new offspring individual is given a position that is based upon the parental position(s) plus some random deviation, as is commonly done, the question arises of how to constrain those new positions; we have already confronted that question, in fact, in the `modifyChild()` callbacks we have used to set offspring positions.

One option is simply to impose no constraint; space is then considered to be infinite in extent in all directions. This is the default in SLiM, simply because SLiM imposes no default constraint; however, it is rarely desirable in individual-based models since a finite population on an infinite landscape has zero density – rarely an interesting or biologically relevant case. Instead, models generally use one of several standard boundary conditions. In this section we will break from our usual conventions and will simply assume all of the code from the previous recipe (section 14.2); here we will present only replacement `modifyChild()` callbacks to implement each of four standard boundary conditions. The literature contains a good deal of discussion of these different boundary conditions and the effects they may have on evolutionary dynamics; we will not review that literature here. We will focus on implementation.

First of all, with "stopping" boundaries, new positions are simply clamped to the spatial boundary; points outside the boundary are forced to the nearest point inside bounds. In SLiM, this can be implemented as:

```
modifyChild() {
    // Stopping boundary conditions
    pos = parent1.spatialPosition + rnorm(2, 0, 0.02);
    child.setSpatialPosition(p1.pointStopped(pos));

    return T;
}
```

This introduces several new concepts. The `spatialPosition` property of `Individual` provides a `float` vector of the spatial coordinates of the individual; since this model has `"xy"` dimensionality, this vector has two elements, with the same values as the `x` and `y` properties that we have been using. The `setSpatialPosition()` is just the reciprocal of this, taking a `float` vector of coordinates and setting them into the `x` and `y` properties of the Individual in one operation, as a convenient shorthand. Finally, the `pointStopped()` method of `Subpopulation` implements the spatial boundary condition by clamping the coordinates in the `float` vector it is passed to the boundaries of the subpopulation and returning the clamped vector. So all in all, this callback gets the coordinates of the parent, adds a normal draw to each (thus deviating the offspring's *x* and *y* coordinates from those of the parent), asks the subpopulation to clamp the new position into bounds, and sets the final position into the child. All of this is just convenient shorthand; it could easily be implemented by using the `x` and `y` properties of the `Individual` directly, as well as the spatial boundaries of the `Subpopulation` (available through its `spatialBounds` property) – it would just be longer, less readable, and more error-prone.

Second, with "reflecting" boundaries, new positions outside the spatial boundary are reflected to fall inside it; the extent to which a point lies outside an edge is translated into the extent to which the point lies inside that edge instead. This requires just a trivial modification of the previous recipe, substituting the `pointReflected()` method in place of `pointStopped()`:

```
modifyChild() {
    // Reflecting boundary conditions
    pos = parent1.spatialPosition + rnorm(2, 0, 0.02);
    child.setSpatialPosition(p1.pointReflected(pos));

    return T;
}
```

Third, with "absorbing" boundaries, new offspring whose proposed positions lie outside bounds are absorbed – their generation is terminated. This is accomplished in SLiM by returning `F` from the `modifyChild()` callback, which tells SLiM to start over from scratch by choosing new parents and generating a completely new offspring:

```
modifyChild() {
    // Absorbing boundary conditions
    pos = parent1.spatialPosition + rnorm(2, 0, 0.02);
    if (!p1.pointInBounds(pos))
       return F;

    child.setSpatialPosition(pos);
    return T;
}
```

This uses the `pointInBounds()` method of Subpopulation to test whether the new position lies inside the spatial boundaries. If not, `F` is returned, terminating generation of the proposed child.

Fourth, with "reprising" boundaries, if a proposed position falls outside bounds a new position is generated until a position within bounds is obtained. This is the boundary condition we implemented the hard way in the previous recipes, but it can be done a little more easily (and more generally, since the spatial boundaries are now not hard-coded):

```
modifyChild() {
    // Reprising boundary conditions
    do pos = parent1.spatialPosition + rnorm(2, 0, 0.02);
    while (!p1.pointInBounds(pos));
    child.setSpatialPosition(pos);

    return T;
}
```

This again uses `pointInBounds()`, but this time if the point is not inside bounds the code loops back to generate a new point, until a point within bounds is obtained.

Finally, with "periodic" boundaries space is constructed in such a manner that boundaries do not exist but the spatial extent is nevertheless finite; the spatial topology is instead cylindrical or toroidal, wrapping around at some or all edges. This boundary condition is a more complex topic than the other boundary conditions, since it actually changes the way in which distances are calculated; we will therefore defer a presentation of it until section 14.12. It's an important topic, though, since periodic boundaries can avoid problematic "edge effects" as discussed there.

We have been using `Subpopulation` methods to check/enforce the boundary conditions for us. `Subpopulation` is the class responsible for landscape-level properties such as the coordinates of the spatial boundaries, as well as other state we will see later. By default the spatial boundaries used by `Subpopulation` span the interval [0,1] in each dimension, and we have allowed that default to stand in the models shown here. This can be changed, using the `setSpatialBounds()` method of `Subpopulation`, but we will not pursue that here (see section 14.7 for an example). In any case, the `Subpopulation` methods we have seen will check and enforce whatever boundaries are set.

One final point worth mentioning is that `Subpopulation` provides a more general way to set up initial random positions. These recipes will use this code to do so:

```
1 late() {
    sim.addSubpop("p1", 500);

    // Initial positions are random within spatialBounds
    for (ind in p1.individuals)
       ind.setSpatialPosition(p1.pointUniform());
}
```

The `pointUniform()` method generates a point drawn at random from within the spatial bounds of the subpopulation (drawing each coordinate from a uniform distribution spanning the range within bounds). This is equivalent to the code presented in earlier recipes, but it will also work properly if the spatial bounds of the subpopulation have been changed from the default, whereas the earlier code would not (since the `[0,1]` interval is hard-coded there).

14.4 Mate choice with a spatial kernel

Now we will work with the "reprising" boundary condition model of section 14.3, and we will add the element of spatial mate choice. The likelihood that one individual will choose another individual as a mate will depend upon the spatial distance between them, falling off with increasing distance according to a Gaussian kernel (but a different one from the competition kernel). This could represent, for example, mate-finding based upon auditory cues such as birdsong which become progressively less perceptible as distance increases.

Doing this is remarkably easy. We just need to add a second interaction type, and utilize it in a `mateChoice()` callback:

```
initialize() {
    initializeSLiMOptions(dimensionality="xy");
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);

    // spatial competition
    initializeInteractionType(1, "xy", reciprocal=T, maxDistance=0.3);
    i1.setInteractionFunction("n", 3.0, 0.1);

    // spatial mate choice
    initializeInteractionType(2, "xy", reciprocal=T, maxDistance=0.1);
    i2.setInteractionFunction("n", 1.0, 0.02);
}
1 late() {
    sim.addSubpop("p1", 500);

    for (ind in p1.individuals)
       ind.setSpatialPosition(p1.pointUniform());
}
1: late() {
    i1.evaluate();
    i2.evaluate();
}
```

```
fitness(NULL) {
    totalStrength = i1.totalOfNeighborStrengths(individual);
    return 1.1 - totalStrength / p1.individualCount;
}
1: mateChoice() {
    // spatial mate choice
    return i2.strength(individual);
}
modifyChild() {
    do pos = parent1.spatialPosition + rnorm(2, 0, 0.02);
    while (!p1.pointInBounds(pos));
    child.setSpatialPosition(pos);

    return T;
}
2000 late() { sim.outputFixedMutations(); }
```

Interaction type `i1` is used for competitive interactions, as before. We now declare `i2` as well, which we will use for mate choice. It also uses a Gaussian kernel, this time with a maximum value of `1.0`, a standard deviation of `0.02`, and a maximum distance of `0.1`. This is quite a narrow, short-range mate-choice function that will promote local mating quite strongly.

Having declared `i2`, we then need to evaluate it in the `1: late()` event, just as we did with `i1`. We are then prepared to use it in the `1: mateChoice()` callback, which simply returns the result of the call `i2.strength(individual)`. This call asks `i2` to evaluate the strength of interaction between the first parent (`individual`) and all other individuals in its subpopulation. The result is returned as a vector. Happily, that is precisely what `mateChoice()` callbacks are expected to return – a vector of mating weights between the first parent and all other individuals. The result can therefore simply be passed on to SLiM without further processing.

That is all that is needed; we now have a model that includes both spatial competition and spatial mate choice, using different kernels. If we run this model in SLiMgui, it looks essentially identical to the model of sections 14.2, but the evolutionary dynamics under the hood are quite different. We can explore that with a quick modification of these recipes, by dropping in the heterozygosity calculator used in section 13.2. The code from the final output event of that recipe can be used without modification. In a quick experiment, we can do 25 runs of the models, run to generation `10000` to allow equilibration, and output the mean nuclear heterozygosity at the end of each run. Let's also do runs of the equivalent non-spatial model (constructed by simply removing all of the interaction code, the `fitness()` callback, the `mateChoice()` callback, and all references to spatial positions). Simple summary statistics across the mean nuclear heterozygosity values obtained from the 25 runs of each of the three models look like this:

Model	Mean	Std. Deviation
Non-spatial	0.0002148	0.000092
Competition only (14.2)	0.0001934	0.000071
Competition and mate choice (14.4)	0.0001005	0.000067

The first thing to note is that the outcomes of the non-spatial and competition-only models are quite similar. Indeed, even with 25 samples each, a *t*-test finds that they do not differ significantly ($p = 0.3651$). Apparently local offspring generation and spatial competition do not suffice to drive much, if any, genetic divergence among spatial clusters. This is not too surprising, since with non-spatial mating in each generation the gene flow blending clusters together is very high.

The second thing to note, however, is that the model with spatial mate choice – this section's recipe – is quite different from the other two. This is confirmed by *t*-test; it is highly significantly different from both the non-spatial model (*p* = 0.0000104) and the competition-only model (*p* = 0.0000204). The addition of spatial mate choice (especially with a narrow kernel) has driven substantial genetic divergence among spatial clusters. We have ourselves a real spatial model.

14.5 Mate choice with a nearest-neighbor search

In this section we will modify the previous recipe to implement spatial mate choice using a nearest-neighbor search instead of a spatial kernel. Each individual choosing a mate will make a choice from among its three nearest neighbors, without further consideration of distance. In this recipe the selection will be random, but it would be simple to make the mate choice depend upon some genetic or non-genetic trait of the prospective mates, reflecting choosy mate selection from within a small pool of nearby candidates.

We will begin with the recipe of section 14.4. To modify it for the present recipe, we need only to replace the `mateChoice()` callback with the following:

```
1: mateChoice() {
    // nearest-neighbor mate choice
    neighbors = i2.nearestNeighbors(individual, 3);
    mates = rep(0.0, p1.individualCount);
    mates[neighbors.index] = 1.0;
    
    return mates;
}
```

The `nearestNeighbors()` method returns the three (`3`) nearest neighbors of the first parent (`individual`). In SLiM, a "neighbor" is an individual within the maximum interaction distance of the focal individual (other than the focal individual itself); individuals beyond that maximum cannot be "neighbors", even if they are the nearest individual to the focal individual. It is therefore possible for this method to return fewer than three individuals; indeed, if `individual` is spatially isolated this method might return an empty vector. The rest of the callback is written with that possibility in mind, however. First, a mating vector is constructed with `0` for all potential mates. Then the values for the neighbors found (if any) are changed to `1`, using the subpopulation indices of the neighbors. Finally, that modified vector is returned. If individual had no neighbors, no indices will be changed, and the returned vector will contain nothing but zeros; this will cause SLiM to draw a new first parent, just as a return value of `float(0)` would.

Note that the `nearestNeighbors()` call is purely a spatial query; it does not involve the calculation of interaction strengths at all. In this recipe, the parameters that configure `i2` – the Gaussian function's maximum value and standard deviation, and indeed the fact that a Gaussian function is to be used at all – are therefore irrelevant and can be removed. The complete recipe:

```
initialize() {
    initializeSLiMOptions(dimensionality="xy");
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
    
    // spatial competition
    initializeInteractionType(1, "xy", reciprocal=T, maxDistance=0.3);
    i1.setInteractionFunction("n", 3.0, 0.1);
```

```
        // spatial mate choice
        initializeInteractionType(2, "xy", reciprocal=T, maxDistance=0.1);
    }
    1 late() {
        sim.addSubpop("p1", 500);

        for (ind in p1.individuals)
          ind.setSpatialPosition(p1.pointUniform());
    }
    1: late() {
        i1.evaluate();
        i2.evaluate();
    }
    fitness(NULL) {
        totalStrength = i1.totalOfNeighborStrengths(individual);
        return 1.1 - totalStrength / p1.individualCount;
    }
    1: mateChoice() {
        // nearest-neighbor mate choice
        neighbors = i2.nearestNeighbors(individual, 3);
        mates = rep(0.0, p1.individualCount);
        mates[neighbors.index] = 1.0;

        return mates;
    }
    modifyChild() {
        do pos = parent1.spatialPosition + rnorm(2, 0, 0.02);
        while (!p1.pointInBounds(pos));
        child.setSpatialPosition(pos);

        return T;
    }
    2000 late() { sim.outputFixedMutations(); }
```

We have now seen three different types of spatial query using `InteractionType`. The first is the use of `totalOfNeighborStrengths()` to add up all of the interactions felt by a focal individual from every other interacting individual; we used this to build spatial competition. The second is `strength()`, which we used to obtain a vector of interaction strengths between the focal individual and all other individuals (it can also calculate the interaction strengths with specific other individuals). And the third is the `nearestNeighbors()` method used here, which returns a vector with (up to) a specified number of the nearest neighbors of a focal individual. `IndividualType` supports several other queries, such as `distance()` to get distances between the focal individual and others, `distanceToPoint()` and `nearestNeighborsOfPoint()` to do those queries using an arbitrary spatial point rather than a focal individual, and `drawByStrength()` to draw neighbors of a focal individual weighted by interaction strength (a fast combination of `nearestNeighbors()`, `strength()`, and `sample()`, conceptually). Instead of providing examples of the use of all these methods – which are all documented in section 21.7.2 – we will now change direction to start building – gradually – towards models of landscape heterogeneity using landscape maps.

14.6 Divergence due to phenotypic competition with an `interaction()` callback

Here we will depart from the previous recipes, which have all used neutral spatial models, to explore a different topic: a non-neutral, non-spatial model. This recipe will involve a quantitative trait, using a strategy similar to that in the recipe of section 13.10. It will use an `InteractionType` to model competition among individuals based upon their phenotype: individuals with a more similar phenotype will compete more strongly (since they utilize similar resources). The goal here is to demonstrate the use of an `interaction()` callback to influence the interaction strengths calculated by SLiM. It is most straightforward to introduce this first in a non-spatial model; in a later section we will see the use of an `interaction()` callback in a spatial model.

This recipe is a first step toward something like the model of Dieckmann & Doebeli (1999): a model demonstrating that phenotypic competition and assortative mating can produce speciation in a non-spatial (i.e. sympatric) model. More specifically, we will be working toward the sexual, "ecological trait" model described in that paper, although our model will be different in many ways – it will be a generational model rather than a continuous-time model, and we will not include the "mating trait" used in that paper, for example. We will continue the development of this model in the next several sections. Here's how we start:

```
initialize() {
    defineConstant("optimum", 5.0);
    defineConstant("sigma_C", 0.4);
    defineConstant("sigma_K", 1.0);

    initializeMutationRate(1e-6);
    initializeMutationType("m1", 0.5, "f", 0.0);        // neutral
    initializeMutationType("m2", 0.5, "n", 0.0, 1.0);   // QTL
    m2.convertToSubstitution = F;

    initializeGenomicElementType("g1", c(m1, m2), c(1, 0.01));
    initializeGenomicElement(g1, 0, 1e5 - 1);
    initializeRecombinationRate(1e-8);
}
1 late() {
    sim.addSubpop("p1", 500);
}
1: late() {
    // construct phenotypes from the additive effects of QTLs
    inds = sim.subpopulations.individuals;
    inds.tagF = inds.sumOfMutationsOfType(m2);
}
fitness(m2) {      // make QTLs intrinsically neutral
    return 1.0;
}
fitness(NULL) {    // reward proximity to the optimum
    return 1.0 + dnorm(optimum - individual.tagF, mean=0.0, sd=sigma_K);
}
1:2001 late() {
    if (sim.generation == 1)
       cat("  gen    mean      sd\n");

    if (sim.generation % 100 == 1)
    {
       tags = p1.individuals.tagF;
       cat(format("%5d  ", sim.generation));
       cat(format("%6.2f  ", mean(tags)));
       cat(format("%6.2f\n", sd(tags)));
    }
}
```

This is a simple model of randomly arising QTLs with additive effects that produce a phenotype; we have seen this sort of model before in sections 13.1 and 13.10 (see those recipes for further discussion). A phenotypic optimum is defined at `5.0`, and a global `fitness()` callback produces stabilizing selection around that optimum by calculating a relative fitness based on divergence from the optimum, using a Gaussian function with a width governed by the defined constant `sigma_K`. The individual QTLs are made effectively neutral with the `fitness(m2)` callback, so that fitness is determined only by the overall phenotype they produce additively. That phenotype is calculated in the `1: late()` event and assigned into the `tagF` properties of the individuals.

Now let's add something new: an interaction to govern phenotypic competition. First, we create the `InteractionType` by adding these lines to the end of the `initialize()` callback:

```
initializeInteractionType(1, "", reciprocal=T);     // competition
i1.setInteractionFunction("f", 1.0);
```

Now `i1` will evaluate our phenotypic competition interaction, which is a reciprocal interaction as in previous recipes. It has a spatiality of `""` because this is a non-spatial model. This means that it has no concept of distance, so the only interaction formula we are allowed to use is a fixed value, type `"f"`. So in its present form this interaction is not terribly useful; every individual interacts with every other individual with a strength of `1.0`. We will fix that momentarily. First, however, let's add code to evaluate the interaction, at the end of the `1: late()` event:

```
// evaluate interactions
i1.evaluate();
```

At this point, let's pause for a moment. We have stabilizing selection toward an optimum at `5.0`, and we start with a mean phenotype of `0.0` since the model starts with no QTLs. At the end of every tenth generation, the output event prints out the generation with the mean and standard deviation of the population's phenotypic values. A typical run looks something like this:

```
 gen    mean     sd
   1    0.00   0.00
 101   -0.00   0.36
 201    0.00   0.12
 301    0.02   0.26
 401   -0.06   0.38
 501   -0.21   1.16
 601   -0.27   0.91
 701    0.12   0.46
 801    0.21   0.38
 901    0.17   0.30
1001    1.26   1.40
1101    4.52   0.46
1201    4.86   0.50
1301    4.87   0.43
1401    4.93   0.48
1501    5.12   0.39
1601    4.96   0.41
1701    4.97   0.39
1801    5.01   0.35
1901    4.84   0.30
2001    4.92   0.27
```

It took a little while for the population to develop enough useful variance to be able to reach the fitness peak, but it got there in the end. The population often contains an appreciable amount of variance in the middle of the evolutionary trajectory, but as it settles onto the optimum the variance decreases and tends toward zero, since any deviation from the phenotypic optimum is punished by the global fitness function. In practice, as seen above, the standard deviation fluctuates around `0.3` or `0.4` for quite a while after the population reaches the optimum.

Now let's finish the model by implementing phenotypic competition. First of all, we will make the interaction i1 more useful by adding an interaction() callback:

```
interaction(i1) {
    return dnorm(exerter.tagF, mean=receiver.tagF, sd=sigma_C) /
      dnorm(0.0, mean=0, sd=sigma_C);
}
```

Since this is the first time we've seen one of these, let's examine it closely. It defines the interaction strength of interaction type i1. It uses two variables, exerter and receiver, that are defined by SLiM; they are pseudo-parameters of the interaction() callback, similar to those we have seen with other types of callbacks. The exerter is the individual exerting the interaction, and the receiver is the individual receiving the interaction; since this interaction is reciprocal, the distinction between the two is arbitrary. The callback looks up the phenotypic values of the two individuals (from their tagF fields) and uses dnorm() to calculate the degree of competition between the two, based upon a Gaussian kernel with width sigma_C. Finally, the interaction strength is normalized to have a maximum value of 1.0 here by dividing by dnorm(0.0, mean=0, sd=sigma_C), so that the maximum strength of competition is independent of the width of the competition kernel.

SLiM will now use this interaction() callback to determine the strength of i1 between every pair of individuals. Note that this callback calculates the strength from scratch; it is also possible for an interaction() callback to modify the default strength calculated by the interaction function, which is supplied to the callback in the pseudo-parameter strength (see section 22.6 on other pseudo-parameters available to interaction() callbacks).

Now, finally, we need to actually use i1 to influence the fitnesses of individuals. We will do that in a global fitness() callback:

```
fitness(NULL) {    // phenotypic competition
    totalStrength = sum(i1.strength(individual));
    return 1.0 - totalStrength / p1.individualCount;
}
```

For each individual, this callback adds up the interaction strengths it feels from every other individual (with sum()), divides by p1.individualCount to get the mean interaction strength, and subtracts that from 1.0 to get a relative fitness value, which is returned. In short, the more competition an individual feels from other individuals of similar phenotype, the lower the individual's fitness will be. If we run this full model now, we see something like:

```
  gen    mean      sd
    1    0.00    0.00
  101    1.62    2.71
  201    4.57    1.38
  301    4.76    1.41
  401    4.87    1.22
  501    4.75    1.44
  ...     ...     ...
 1301    4.98    1.38
 1401    5.04    1.60
 1501    5.43    1.61
 1601    5.01    1.32
 1701    5.20    1.30
 1801    5.50    1.78
 1901    5.22    1.39
 2001    5.54    1.75
```

Note that the phenotypic variance rises to higher levels now, and stays high for the remainder of the run. The theoretical expectation is that the variance will remain high indefinitely because the presence of phenotypic competition rewards divergence from the mean phenotype.

A key point to understand regarding this model is that the `interaction()` callbacks will be called while fitness values are being calculated, as a side effect of the `i1.strength()` call in the global `fitness()` callback. When `evaluate()` is called on an `InteractionType`, the positions of all individuals are saved in a snapshot, and distances and interaction strengths are calculated based upon that snapshot. When `interaction()` callbacks are involved, however, they are called in a deferred fashion because they are slow; calling them may not be necessary at all, if particular interaction strengths are never queried, so deferring the calls can provide a very large performance gain. It is admittedly strange, however, that `interaction()` callbacks are called at a later time than the "official" evaluation of the interaction; indeed, they can be called up until mating begins in the following generation, depending upon when the model queries the interaction. If this fact proves difficult to manage in a model, it is possible to supply an `immediate=T` option to `evaluate()` that forces all interactions to be fully and synchronously evaluated at that point, including callouts to all `interaction()` callbacks. This is not necessary in this model, since having `interaction()` callbacks get called during fitness evaluation poses no logistical difficulties; but this is a point worth keeping in mind when developing your own `interaction()` callbacks.

The full model looks like this:

```
initialize() {
    defineConstant("optimum", 5.0);
    defineConstant("sigma_C", 0.4);
    defineConstant("sigma_K", 1.0);

    initializeMutationRate(1e-6);
    initializeMutationType("m1", 0.5, "f", 0.0);        // neutral
    initializeMutationType("m2", 0.5, "n", 0.0, 1.0);   // QTL
    m2.convertToSubstitution = F;

    initializeGenomicElementType("g1", c(m1, m2), c(1, 0.01));
    initializeGenomicElement(g1, 0, 1e5 - 1);
    initializeRecombinationRate(1e-8);

    initializeInteractionType(1, "", reciprocal=T);     // competition
    i1.setInteractionFunction("f", 1.0);
}
1 late() {
    sim.addSubpop("p1", 500);
}
1: late() {
    // construct phenotypes from the additive effects of QTLs
    inds = sim.subpopulations.individuals;
    inds.tagF = inds.sumOfMutationsOfType(m2);

    // evaluate interactions
    i1.evaluate();
}
fitness(m2) {      // make QTLs intrinsically neutral
    return 1.0;
}
fitness(NULL) {    // reward proximity to the optimum
    return 1.0 + dnorm(optimum - individual.tagF, mean=0.0, sd=sigma_K);
}
```

```
interaction(i1) {
    return dnorm(exerter.tagF, mean=receiver.tagF, sd=sigma_C) /
      dnorm(0.0, mean=0, sd=sigma_C);
}
fitness(NULL) {    // phenotypic competition
    totalStrength = sum(i1.strength(individual));
    return 1.0 - totalStrength / p1.individualCount;
}
1:2001 late() {
    if (sim.generation == 1)
      cat("  gen    mean      sd\n");

    if (sim.generation % 100 == 1)
    {
      tags = p1.individuals.tagF;
      cat(format("%5d  ", sim.generation));
      cat(format("%6.2f  ", mean(tags)));
      cat(format("%6.2f\n", sd(tags)));
    }
}
```

Since this model does not include assortative mating, it is not expected to produce speciation (and we will see in the next section that it does not). At present, it is merely a model of what Haller & Hendry (2013) called "squashed stabilizing selection": selection based upon a fitness function that is stabilizing around an optimum, but has been squashed downward at its center due to negative frequency-dependent selection, producing disruptive selection that nevertheless keeps the population in the vicinity of the fitness peak. We will add assortative mating to this model in the recipe of section 14.8, but first, let's examine a way to improve upon the model as it now stands.

14.7 Modeling phenotype as a spatial dimension

In the previous section, we built a model of a quantitative trait constructed from randomly arising QTLs that combined additively to determine the phenotype. We then built an interaction to model competition based upon similarity in phenotype. In this section we will modify that recipe slightly, to better utilize the power of `InteractionType`. Although this model will remain a non-spatial model for the time being, we will now model the phenotype in SLiM as if it were a spatial dimension. This will bring us two benefits: speed, and additional visualization power.

This change is quite straightforward. Beginning with the model of section 14.6, we first need to enable spatiality at the beginning of the `initialize()` callback:

```
initializeSLiMOptions(dimensionality="x");
```

We will use the `x` property of individuals to store their phenotypes now, instead of `tagF`:

```
inds.x = inds.sumOfMutationsOfType(m2);
```

The `fitness()` callback that enforces the phenotypic optimum should change to use `x`:

```
fitness(NULL) {    // reward proximity to the optimum
    return 1.0 + dnorm(optimum - individual.x, mean=0.0, sd=sigma_K);
}
```

The `interaction()` callback also needs the same change:

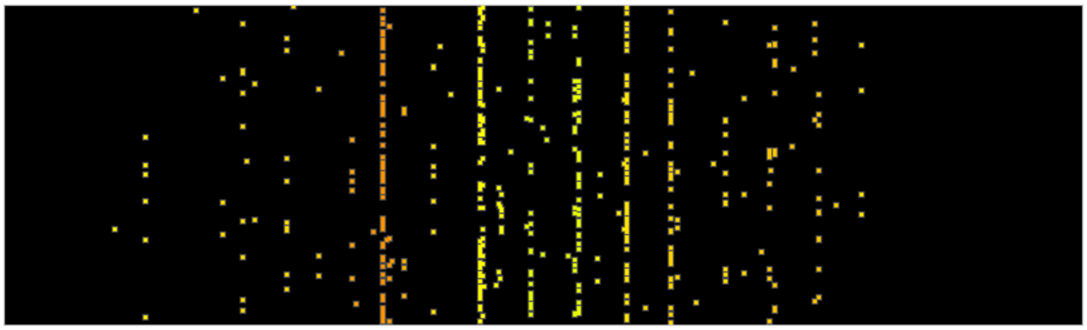
```
    interaction(i1) {
        return dnorm(exerter.x, mean=receiver.x, sd=sigma_C) /
          dnorm(0.0, mean=0, sd=sigma_C);
    }
```

Finally, the output code should also use `x` instead of `tagF` (see the full model below).

Let's make one other change. Previously, we've seen two-dimensional spatial models that used the default boundaries of [0, 1] in *x* and *y*. In section 14.3 we mentioned that this default could be changed; let's change it now, because in this model phenotypic values often go outside that range. We can add a line immediately after `p1` is defined, telling `p1` its spatial boundaries:

```
    p1.setSpatialBounds(c(0.0, 10.0));
```

That's it; we now have a model in which phenotype is considered to be a pseudo-spatial dimension. Why is this model better? The first reason is that it provides us with better visualization capabilities in SLiMgui. If we run the model now, we get a display that shows individuals in a one-dimensional phenotypic space (with random *y* coordinates chosen by SLiM to spread the individuals out for greater visibility):



Since we told `p1` that its spatial boundaries were [0.0, 10.0], that is the spatial extent displayed by SLiMgui here, so the phenotypic optimum is at the horizontal center of the display here. This snapshot, taken at about generation `300`, shows that the population has already reached the optimum; the mean phenotype here is `4.91`, in fact, with a standard deviation of `1.40` – typical of the model's equilibrium state. Colors correspond to fitness as usual; the band of individuals on the left is particularly low-fitness because it is far off of the optimum, and yet is also quite crowded – there are a lot of individuals with that phenotype at this instant in time. All of the discrete banding here is the result of variation in QTLs of relatively large effect. Note that individuals quite far off the fitness peak can still be fairly high-fitness, as long as their phenotype is rare.

So this is one benefit of treating phenotype as a spatial dimension: the dynamic evolution of the phenotypic distribution can be watched in real time, color-coded by fitness as the fitness function resulting from the squashed stabilizing selection fluctuates from generation to generation.

The other benefit is that the model is much faster, because `InteractionType`'s optimizations for spatial interactions are brought to bear. First, if we realize that the Gaussian phenotypic competition function we're presently simulating with an `interaction()` callback is equivalent to one of SLiM's built-in interaction functions, then we can completely remove the `interaction()` callback. We then need to change the definition of the `i1` interaction like so:

```
    initializeInteractionType(1, "x", reciprocal=T, maxDistance=sigma_C * 3);
    i1.setInteractionFunction("n", 1.0, sigma_C);
```

This defines `i1` as a spatial interaction using `x`, which is our phenotypic "dimension". It then tells `i1` to use a Gaussian function with a maximum value of `1.0` and a width of `sigma_C` –

precisely what the `interaction()` callback used to do. Indeed, this model is exactly equivalent; running it with the same random number seed produces the same result as shown in the snapshot above. The difference is that it runs much faster – it completes about `4750` generations in `30` seconds (on my machine), whereas the version using an `interaction()` callback completes about `420` generations in `30` seconds. Not a bad speed improvement! The key is that we have avoided having to make a call to an Eidos `interaction()` callback for every interaction, which is slow.

Indeed, even a little more speed can be squeezed out, at the price of accuracy. If a maximum distance of `0.8` is set for `i1`, and `totalOfNeighborStrengths()` is used instead of `strength()` in the global `fitness()` callback that calculates phenotypic competition, about `5030` generations can be completed in `30` seconds. Since a maximum distance of `0.8` is two standard deviations of the competition kernel, the effects of this change should be relatively small in terms of the overall behavior of the model, but it is nevertheless a sacrifice in accuracy, and the performance gain in this case is not large, so we will not consider this change to be a part of the official recipe for this section. In other cases, however, the performance gain can be very large; a maximum distance should always be considered for spatial interactions, particularly if it can safely be set to a short enough distance to exclude most other individuals from interacting with the focal individual at all.

The full recipe for this section, for posterity, is:

```
initialize() {
    defineConstant("optimum", 5.0);
    defineConstant("sigma_C", 0.4);
    defineConstant("sigma_K", 1.0);

    initializeSLiMOptions(dimensionality="x");
    initializeMutationRate(1e-6);
    initializeMutationType("m1", 0.5, "f", 0.0);        // neutral
    initializeMutationType("m2", 0.5, "n", 0.0, 1.0);   // QTL
    m2.convertToSubstitution = F;

    initializeGenomicElementType("g1", c(m1, m2), c(1, 0.01));
    initializeGenomicElement(g1, 0, 1e5 - 1);
    initializeRecombinationRate(1e-8);

    initializeInteractionType(1, "x", reciprocal=T,
      maxDistance=sigma_C * 3);     // competition
    i1.setInteractionFunction("n", 1.0, sigma_C);
}
1 late() {
    sim.addSubpop("p1", 500);
    p1.setSpatialBounds(c(0.0, 10.0));
}
1: late() {
    // construct phenotypes from the additive effects of QTLs
    inds = sim.subpopulations.individuals;
    inds.x = inds.sumOfMutationsOfType(m2);

    // evaluate interactions
    i1.evaluate();
}
fitness(m2) {      // make QTLs intrinsically neutral
    return 1.0;
}
fitness(NULL) {    // reward proximity to the optimum
    return 1.0 + dnorm(optimum - individual.x, mean=0.0, sd=sigma_K);
}
```

```
fitness(NULL) {    // phenotypic competition
    totalStrength = sum(i1.strength(individual));
    return 1.0 - totalStrength / p1.individualCount;
}
1:2001 late() {
    if (sim.generation == 1)
      cat("  gen    mean      sd\n");

    if (sim.generation % 100 == 1)
    {
      tags = p1.individuals.x;
      cat(format("%5d  ", sim.generation));
      cat(format("%6.2f  ", mean(tags)));
      cat(format("%6.2f\n", sd(tags)));
    }
}
```

14.8 Sympatric speciation facilitated by assortative mating

In the previous section we refined our non-spatial model of phenotypic competition, by treating phenotype as though it were a spatial dimension so that SLiM could run the model more quickly and with better visualization. It is now time to take another step toward the model of Dieckmann & Doebeli (1999) by changing mating in the model to be assortative by phenotype. This will in some ways be similar to what we did in section 14.4; but there mating was spatially assortative, whereas here mating will be phenotypically assortative.

Beginning with the model of section 14.7, the changes needed are quite small. First, we need to add code in our `initialize()` callback to define a new interaction type, `i2`, that we will use to evaluate mates:

```
initializeInteractionType(2, "x", reciprocal=T, maxDistance=sigma_M * 3);
i2.setInteractionFunction("n", 1.0, sigma_M);
```

We have to add a definition of the `sigma_M` kernel width as well, at the beginning of the `initialize()` callback:

```
defineConstant("sigma_M", 0.5);
```

Since this interaction is based on `"x"`, which is our pseudo-spatial phenotype dimension, it represents phenotypic proximity just as `i1`, our phenotypic competition interaction, does. Indeed, the only reason not to use `i1` to govern mate choice as well is that we want to be able to make it use a different interaction function than competition, so that we can play with the width of the mate-choice kernel independently of the width of the competition kernel.

Next, we need to evaluate that interaction in our `1: late()` event every generation:

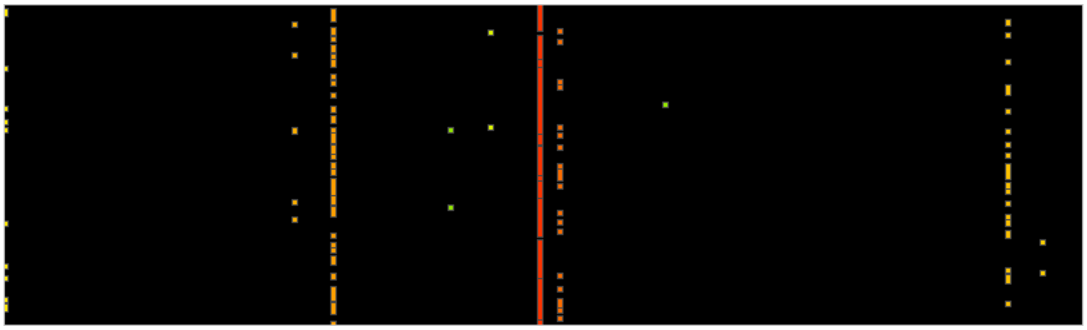
```
i2.evaluate();
```

And finally, we need a mate choice callback that uses that interaction:

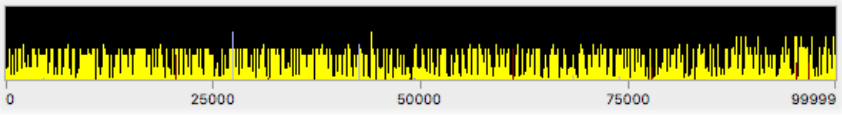
```
mateChoice() {
    // spatial mate choice
    return i2.strength(individual);
}
```

And that's it. We now have a model in which phenotype, as determined by randomly arising additive QTLs, is something like a "magic trait" (Servedio et al. 2011) – a trait that simultaneously determines both fitness (because of the phenotypic optimum) and assortative mating (because of the `mateChoice()` callback) (although it is perhaps not strictly a magic trait since it is governed by underlying QTLs; see sections 11.1 and 13.1 for more discussion of this topic). When exposed to the disruptive selection caused by phenotypic competition in the model, the magic-ish trait here readily produces speciation. (Note that this is true speciation, not evolutionary branching, because this is a sexual model in the sense that matters – biparental mating with assortment and recombination of gametes – even though it models hermaphrodites, not separate sexes).

We can see evidence for speciation in two different ways in SLiMgui. First of all, instead of the cloud of different phenotypes around the optimum that the previous model generated, we now see a set of discrete phenotypic clusters:



Second, we now see strong genetic separation between these clusters in the pattern of neutral variation exhibited by the population:



Note that there are no neutral mutations at high frequency at all; instead, there is a large amount of neutral diversity that is pinned at a couple of intermediate frequencies. These are blocs of neutral mutations that have fixed within one of the species in the model, but are unable to spread more widely because of the reproductive isolation between the species. Hybridization is not impossible; it does occur occasionally, as can be seen in the snapshot above. But it is rare enough that gene flow between the species is insufficient to allow that neutral diversity to spread.

It would be fair to argue that although this is a model of speciation given a pre-existing magic trait, it is not a model of the emergence of the magic trait itself, because it lacks the "mating trait" of the Dieckmann & Doebeli (1999) model. Adding in such a trait would be a simple extension of the present model, and would presumably support the result found by Dieckmann & Doebeli (1999) – that in an ecological scenario such as this, assortative mating will readily emerge, transforming an ordinary trait into a magic trait that then facilitates speciation. We will leave that extension of the model as an exercise for the reader, since pursuing it would not serve the aims of this chapter. Instead, in the next section we will turn back toward spatial models, while incorporating what we have done here with QTLs and phenotype-based competition and mating.

Here's the full model, for the record:

```
initialize() {
    defineConstant("optimum", 5.0);
    defineConstant("sigma_C", 0.4);
    defineConstant("sigma_K", 1.0);
    defineConstant("sigma_M", 0.5);

    initializeSLiMOptions(dimensionality="x");
    initializeMutationRate(1e-6);
    initializeMutationType("m1", 0.5, "f", 0.0);        // neutral
    initializeMutationType("m2", 0.5, "n", 0.0, 1.0);   // QTL
    m2.convertToSubstitution = F;

    initializeGenomicElementType("g1", c(m1, m2), c(1, 0.01));
    initializeGenomicElement(g1, 0, 1e5 - 1);
    initializeRecombinationRate(1e-8);

    initializeInteractionType(1, "x", reciprocal=T,
      maxDistance=sigma_C * 3);     // competition
    i1.setInteractionFunction("n", 1.0, sigma_C);

    initializeInteractionType(2, "x", reciprocal=T,
      maxDistance=sigma_M * 3);     // mate choice
    i2.setInteractionFunction("n", 1.0, sigma_M);
}
1 late() {
    sim.addSubpop("p1", 500);
    p1.setSpatialBounds(c(0.0, 10.0));
}
1: late() {
    // construct phenotypes from the additive effects of QTLs
    inds = sim.subpopulations.individuals;
    inds.x = inds.sumOfMutationsOfType(m2);

    // evaluate interactions
    i1.evaluate();
    i2.evaluate();
}
fitness(m2) {      // make QTLs intrinsically neutral
    return 1.0;
}
fitness(NULL) {    // reward proximity to the optimum
    return 1.0 + dnorm(optimum - individual.x, mean=0.0, sd=sigma_K);
}
fitness(NULL) {    // phenotypic competition
    totalStrength = sum(i1.strength(individual));
    return 1.0 - totalStrength / p1.individualCount;
}
mateChoice() {
    // spatial mate choice
    return i2.strength(individual);
}
1:5001 late() {
    if (sim.generation == 1)
      cat("  gen    mean      sd\n");

    if (sim.generation % 100 == 1)
    {
      tags = p1.individuals.x;
      cat(format("%5d  ", sim.generation));
      cat(format("%6.2f  ", mean(tags)));
      cat(format("%6.2f\n", sd(tags)));
    }
}
```

14.9 Speciation due to spatial variation in selection

In the previous section, we observed that speciation can occur as a result of phenotypic competition and assortative mate choice in a non-spatial model. In this section we will return to spatial modeling, while preserving many aspects of the previous recipe. We will now introduce spatial variation in selection, and will observe adaptive speciation among spatial groups as a result of local selection pressures in combination with phenotypic competition. The optimum trait value for the quantitative trait – the phenotypic optimum, in other words – will vary according to the *x* position in space, producing a linear environmental gradient. This model is broadly inspired by the model of Doebeli & Dieckmann (2003), although again there are many differences.

This recipe has enough differences from the previous recipe that we will build it here from scratch, rather than just giving changes relative to the previous recipe. Let's start with the setup:

```
initialize() {
    defineConstant("sigma_C", 0.1);
    defineConstant("sigma_K", 0.5);
    defineConstant("sigma_M", 0.1);
    defineConstant("slope", 1.0);
    defineConstant("N", 500);

    initializeSLiMOptions(dimensionality="xyz");
    initializeMutationRate(1e-6);
    initializeMutationType("m1", 0.5, "f", 0.0);        // neutral
    initializeMutationType("m2", 0.5, "n", 0.0, 1.0);   // QTL
    m2.convertToSubstitution = F;

    initializeGenomicElementType("g1", c(m1, m2), c(1, 0.1));
    initializeGenomicElement(g1, 0, 1e5 - 1);
    initializeRecombinationRate(1e-8);

    initializeInteractionType(1, "xyz", reciprocal=T,
      maxDistance=sigma_C * 3);     // competition
    i1.setInteractionFunction("n", 1.0, sigma_C);

    initializeInteractionType(2, "xyz", reciprocal=T,
      maxDistance=sigma_M * 3);     // mate choice
    i2.setInteractionFunction("n", 1.0, sigma_M);
}
1 late() {
    sim.addSubpop("p1", N);
    p1.setSpatialBounds(c(0.0, 0.0, -slope, 1.0, 1.0, slope));

    for (ind in p1.individuals)
      ind.setSpatialPosition(p1.pointUniform());
    p1.individuals.z = 0.0;
}
```

This model is our first to use dimensionality "xyz". The *x* and *y* dimensions are true spatial dimensions; this is a 2-D model. The *z* dimension will be used here for phenotype, just as we used *x* as a pseudo-spatial phenotypic dimension in previous recipes. We set up QTL machinery for the phenotype much as we did before; the fraction of mutations that are QTLs is higher in this model just so that we don't have to wait as long to get interesting behavior. We create two interaction types, i1 for competition and i2 for mating, as before. Note that both of these interaction types have spatiality "xyz"; i1 therefore encompasses both spatial and phenotypic competition in a single interaction, and i2 encompasses both spatially and phenotypically assortative mate choice. For our purposes here this is sufficient, but more interaction types could be defined as desired.

Then we set up the population, in the `1 late()` event. We set spatial boundaries of `[0.0, 1.0]` for *x* and *y*, and of `[-slope, slope]` for *z*. The optimum phenotype will actually vary from `-slope/2` to `slope/2`, from the left edge to the right edge of the environment; the wider interval here is used just to allow for some phenotypic variation beyond that interval. (In fact, the spatial boundary for *z* is not used in this model, nor by SLiMgui, so it is irrelevant anyway). Finally, we set random spatial positions for all of the initial individuals, and zero out their phenotypes.

Next, let's implement the machinery to manage spatial positions and phenotypes:

```
modifyChild() {
    // set offspring position based on parental position
    do
       pos = c(parent1.spatialPosition[0:1] + rnorm(2, 0, 0.005), 0.0);
    while (!p1.pointInBounds(pos));
    child.setSpatialPosition(pos);

    return T;
}
1: late() {
    // construct phenotypes from the additive effects of QTLs
    inds = sim.subpopulations.individuals;
    phenotype = inds.sumOfMutationsOfType(m2);
    inds.z = phenotype;

    // color individuals according to phenotype
    for (ind in inds)
    {
       hue = ((ind.z + slope) / (slope * 2)) * 0.66;
       ind.color = rgb2color(hsv2rgb(c(hue, 1.0, 1.0)));
    }

    // evaluate interactions
    i1.evaluate();
    i2.evaluate();
}
```

As in previous recipes, we use a `modifyChild()` callback to place offspring near their first parent, with a small random deviation. We ensure that the offspring phenotype is `0.0` here, so that it doesn't cause the `pointInBounds()` call to return `F`; we don't want SLiM to bounds-check offspring phenotypes for us. The phenotype of `0.0` set here is overwritten a moment later, in the `1: late()` event above, when phenotypes are calculated for all individuals and placed into their *z* coordinate. A bit of extra code here calculates color values for individuals; in this model individuals are colored according to their phenotype, rather than their fitness, so that spatial adaptive divergence is directly visible in SLiMgui, as we'll see below. The code here calculates a hue in the HSV (hue/saturation/value) color system, then converts that to the RGB (red/green/blue) color system and then to a hexadecimal color string which it sets as the color of the individual (see the Eidos manual for details on these functions). Finally, the two interaction types are evaluated.

Next, let's add all of our fitness callbacks and other interaction-related machinery:

```
fitness(m2) {      // make QTLs intrinsically neutral
    return 1.0;
}
fitness(NULL) {    // reward proximity to the optimum
    optimum = (individual.x - 0.5) * slope;
    return 1.0 + dnorm(optimum - individual.z, mean=0.0, sd=sigma_K);
}
```

```
    fitness(NULL) {    // phenotypic competition
        totalStrength = sum(i1.strength(individual));
        return 1.0 - totalStrength / p1.individualCount;
    }
    mateChoice() {
        // spatial mate choice
        return i2.strength(individual);
    }
```

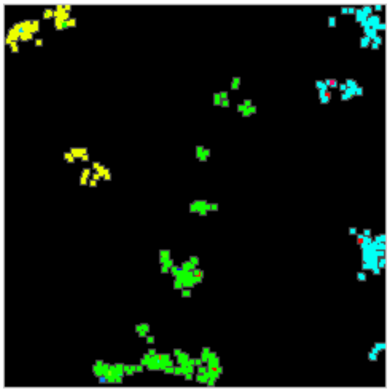
The m2 `fitness()` callback zeroes out the individual fitness effects of our QTLs, as usual. The first global `fitness()` callback rewards individuals for proximity to the fitness optimum; in previous recipes the optimum was a constant value, but now the optimum depends upon the individual's position in space, since we are now modeling a linear spatial environmental gradient. Apart from the fact that the optimum now depends upon `individual.x` and `slope`, this is much the same as before. The second global `fitness()` callback implements competition, both spatial and phenotypic; it is actually unchanged from the previous recipe. Similarly, the `mateChoice()` callback is unchanged, although it now scores mates based upon both spatial and phenotypic similarity.

Finally, let's use the same output event that we used before:

```
    1:5001 late() {
        if (sim.generation == 1)
           cat("  gen    mean      sd\n");

        if (sim.generation % 100 == 1)
        {
           tags = p1.individuals.z;
           cat(format("%5d  ", sim.generation));
           cat(format("%6.2f  ", mean(tags)));
           cat(format("%6.2f\n", sd(tags)));
        }
    }
```

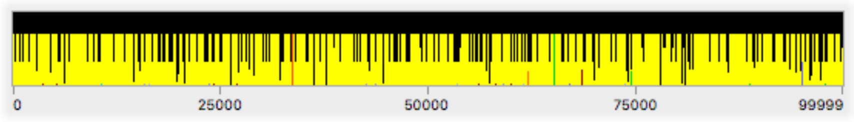
This prints out a history of the phenotypic mean and standard deviation every `100` generations.

Running this model does indeed produce speciation. One sign of that is that we can see discrete clusters of individuals of different colors, representing the fact that they have adapted to different parts of the environmental gradient:



There are three species present here, colored yellow, green, and cyan, adapted to the conditions at the left, center, and right of the environmental gradient, respectively. (There are also a few mutants of other colors sprinkled in.)

Another piece of evidence for speciation is the presence of large amounts of neutral diversity that is not mixing between the different phenotypic clusters, as we saw before in section 14.8:



Many mutations are at a frequency of approximately 2/3 because they are shared between two species; the yellow species split from the green species only about `1000` generations before these snapshots were taken, and so the two species share a great deal of their genetic background. Many other mutations are at a frequency of approximately 1/3 because they are shared only within the cyan species, which split from the green species more than `8000` generations earlier. Remarkably, not a single mutation has fixed across the whole population after `9000` generations of runtime; the onset of speciation is quite early (in this run of the model, at least), and the reproductive barrier is quite strong with the parameter values used here.

One could bring in other machinery to further assess the extent of adaptive divergence and reproductive isolation, such as the F_{ST} calculation code we've used in a couple of recipes before. Indeed, one could dump out the neutral diversity to a file and run a STRUCTURE analysis on it to see whether the groups that appear to be species fall out as genetic clusters naturally. We won't pursue that here since the divergence is so readily apparent.

The full model, for reference:

```
initialize() {
    defineConstant("sigma_C", 0.1);
    defineConstant("sigma_K", 0.5);
    defineConstant("sigma_M", 0.1);
    defineConstant("slope", 1.0);
    defineConstant("N", 500);

    initializeSLiMOptions(dimensionality="xyz");
    initializeMutationRate(1e-6);
    initializeMutationType("m1", 0.5, "f", 0.0);        // neutral
    initializeMutationType("m2", 0.5, "n", 0.0, 1.0);   // QTL
    m2.convertToSubstitution = F;

    initializeGenomicElementType("g1", c(m1, m2), c(1, 0.1));
    initializeGenomicElement(g1, 0, 1e5 - 1);
    initializeRecombinationRate(1e-8);

    initializeInteractionType(1, "xyz", reciprocal=T,
       maxDistance=sigma_C * 3);     // competition
    i1.setInteractionFunction("n", 1.0, sigma_C);

    initializeInteractionType(2, "xyz", reciprocal=T,
       maxDistance=sigma_M * 3);     // mate choice
    i2.setInteractionFunction("n", 1.0, sigma_M);
}
1 late() {
    sim.addSubpop("p1", N);
    p1.setSpatialBounds(c(0.0, 0.0, -slope, 1.0, 1.0, slope));

    for (ind in p1.individuals)
       ind.setSpatialPosition(p1.pointUniform());
    p1.individuals.z = 0.0;
}
```

```
modifyChild() {
    // set offspring position based on parental position
    do
       pos = c(parent1.spatialPosition[0:1] + rnorm(2, 0, 0.005), 0.0);
    while (!p1.pointInBounds(pos));
    child.setSpatialPosition(pos);

    return T;
}
1: late() {
    // construct phenotypes from the additive effects of QTLs
    inds = sim.subpopulations.individuals;
    phenotype = inds.sumOfMutationsOfType(m2);
    inds.z = phenotype;

    // color individuals according to phenotype
    for (ind in inds)
    {
       hue = ((ind.z + slope) / (slope * 2)) * 0.66;
       ind.color = rgb2color(hsv2rgb(c(hue, 1.0, 1.0)));
    }

    // evaluate interactions
    i1.evaluate();
    i2.evaluate();
}
fitness(m2) {      // make QTLs intrinsically neutral
    return 1.0;
}
fitness(NULL) {    // reward proximity to the optimum
    optimum = (individual.x - 0.5) * slope;
    return 1.0 + dnorm(optimum - individual.z, mean=0.0, sd=sigma_K);
}
fitness(NULL) {    // phenotypic competition
    totalStrength = sum(i1.strength(individual));
    return 1.0 - totalStrength / p1.individualCount;
}
mateChoice() {
    // spatial mate choice
    return i2.strength(individual);
}
1:5001 late() {
    if (sim.generation == 1)
       cat("  gen    mean      sd\n");

    if (sim.generation % 100 == 1)
    {
       tags = p1.individuals.z;
       cat(format("%5d  ", sim.generation));
       cat(format("%6.2f  ", mean(tags)));
       cat(format("%6.2f\n", sd(tags)));
    }
}
```

14.10 A simple biogeographic landscape model

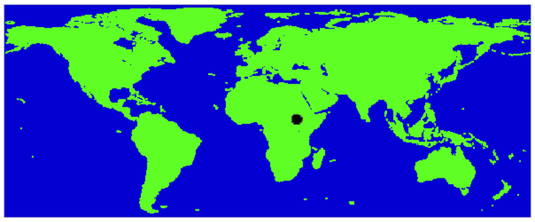
The time has come to introduce a new topic: landscape maps. For this, we will temporarily abandon the spatial quantitative-trait local adaptation model we have been building, and switch to a much simpler model. Our goal in this section is to build a simple biogeographic model that uses a landscape map. Just for fun, the map we will use is a map of the world. There are no end of issues with this – the map projection distorts the geography, Russia and Alaska are not connected across the Bering Strait because the spatial boundary intervenes, and so forth. But as a simple toy model to illustrate the concept and the potential of landscape maps, it should serve our purposes.

Let's start with the model, and then delve into the concepts:

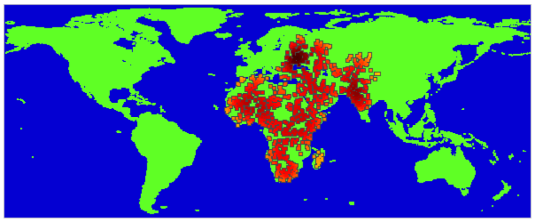
```
initialize() {
    initializeSLiMOptions(dimensionality="xy");
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);

    // spatial competition
    initializeInteractionType(1, "xy", reciprocal=T, maxDistance=30.0);
    i1.setInteractionFunction("n", 5.0, 10.0);

    // spatial mate choice
    initializeInteractionType(2, "xy", reciprocal=T, maxDistance=30.0);
    i2.setInteractionFunction("n", 1.0, 10.0);
}
1 late() {
    sim.addSubpop("p1", 1000);

    p1.setSpatialBounds(c(0.0, 0.0, 540.0, 217.0));

    mapLines = rev(readFile("~/Desktop/world_map_540x217.txt"));
    mapLines = sapply(mapLines, "strsplit(applyValue, '') == '#';");
    mapValues = asFloat(mapLines);

    p1.defineSpatialMap("world", "xy", c(540, 217), mapValues,
       valueRange=c(0.0, 1.0), colors=c("#0000CC", "#55FF22"));

    // start near a specific map location
    for (ind in p1.individuals) {
       ind.x = rnorm(1, 300.0, 1.0);
       ind.y = rnorm(1, 100.0, 1.0);
    }
}
1: late() {
    i1.evaluate();
    i2.evaluate();
}
fitness(NULL) {
    comp = i1.totalOfNeighborStrengths(individual) / p1.individualCount;
    comp = min(c(comp, 0.99));
    return 1.0 - comp;
}
1: mateChoice() {
    return i2.strength(individual);
}
```

```
modifyChild() {
    do pos = parent1.spatialPosition + rnorm(2, 0, 2.0);
    while (!p1.pointInBounds(pos));

    // prevent dispersal into water
    if (p1.spatialMapValue("world", pos) == 0.0)
      return F;

    child.setSpatialPosition(pos);
    return T;
}
20000 late() { sim.outputFixedMutations(); }
```

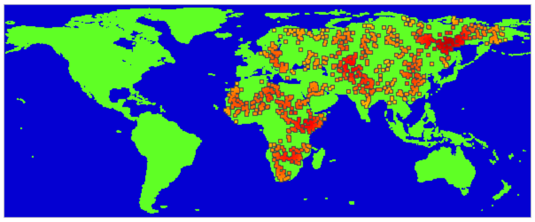
Here's what the model looks like in SLiMgui at the end of generation `1`, right after the population has been set up:



The black dot in eastern Africa is the initial population; this model seeds the population at a specific location, perhaps simulating – not realistically, obviously! – the origin of *Homo sapiens* in Africa. This model has spatial competition and spatial mate choice, as we have seen in previous recipes, so the population rapidly spreads to occupy new territory in order to escape the local competition from other individuals. Here is the population at the end of generation `63`:



Notice that the individuals are constrained to occupy only land locations. It is also interesting that they have managed to reach Madagascar; the dispersal kernel used can jump small distances, so the population can sometimes bridge the Mozambique Channel. Some water gaps are too large to bridge, however. Here is the population at the end of generation `1000`:



The population has spread across all of mainland Asia, but has not been able to enter Indonesia, and has thus not reached Australia; the land area provided by the Indonesian islands is probably too small to support a subpopulation (and similarly, the subpopulation that colonized Madagascar has died out). Reaching the New World would be even more difficult, given the fact that the Bering Strait is unavailable (a periodic boundary condition in the *x* direction would be needed to make that work); individuals would have to make like the Vikings and jump from mainland Europe to Iceland, Greenland, and thence to North America.

The fact that this particular biogeographic pattern is observed is not necessarily a problem, of course; a great many organisms are unable to disperse from Eurasia to Australia or the Americas. But it is a consequence of the details of this model – the particular dispersal kernel chosen, the particular way in which dispersal is constrained to land, the details of the map used (the fact that it does not include elevation, rivers, etc.), the way in which competition and mating are implemented, and so forth. There is no obstacle to changing these details to match the biological details of a particular species, to produce a more empirically based biogeographic model.

So, how was this recipe constructed? Let's now delve into a few of the details. Most of the model is familiar boilerplate: the setup in `initialize()`, the `1: late()` event that evaluates the spatial interactions, and the `fitness()` and `mateChoice()` callbacks, for example. Let's start, then, by looking at the `1 late()` event that initializes the population:

```
1 late() {
    sim.addSubpop("p1", 1000);

    p1.setSpatialBounds(c(0.0, 0.0, 540.0, 217.0));

    mapLines = rev(readFile("~/Desktop/world_map_540x217.txt"));
    mapLines = sapply(mapLines, "strsplit(applyValue, '') == '#';");
    mapValues = asFloat(mapLines);

    p1.defineSpatialMap("world", "xy", c(540, 217), mapValues,
       valueRange=c(0.0, 1.0), colors=c("#0000CC", "#55FF22"));

    // start near a specific map location
    for (ind in p1.individuals) {
       ind.x = rnorm(1, 300.0, 1.0);
       ind.y = rnorm(1, 100.0, 1.0);
    }
}
```

It begins by creating a subpopulation, `p1`, as usual. It then sets up spatial boundaries for `p1`, from (0, 0) to (540, 217); this is dictated by the size of the map that we are about to load, which is 540x217 pixels in size. The spatial bounds do not need to match that, but it is usually desirable for them to at least match the aspect ratio of the map, so that the map is not stretched.

The map is then read in from a file; note that the path to this file will probably be different on your system (it can be found inside the Recipes folder that can be downloaded from SLiM's home page). This is just a simple text file; each line is comprised of a series of spaces and hash marks ("`#`"), where the hash marks indicate land. If you open this file in a text editor and view it in a monospace font at a very small point size (like 3 pt), you will see the world map. It is read with `readFile()`, which returns a vector of `string` objects representing the lines of the file.

SLiM uses Cartesian coordinates for spatial models, which means that *x* increases to the right and *y* increases to the top. Our world map, on the other hand, is rendered from top to bottom, as is common for pixel-based image formats. We use the `rev()` function to reverse the order of the lines in the map so that it matches SLiM's coordinate system. We then use `sapply()` and `strsplit()` to split each line into individual characters, and then convert those into `logical` values – `T` for land, `F` for water. Finally, these `logical` values are converted to `float`, according to the Eidos rule that `T` is `1` and `F` is `0`. The map, now in `mapValues`, is now ready for use.

Now we call the `defineSpatialMap()` method of Subpopulation to give the map to SLiM. The first parameter, `"world"`, is a name for the map; you can define as many spatial maps as you wish, and you refer to them by name. The `"xy"` parameter indicates the spatiality of the map, which must be a subset of the dimensionality of the model as a whole; here our map covers dimensions *x* and *y*. Next we give the dimensions of the map, in pixels; it is 540x217, because those are the dimensions of the data we read from the file. Next we provide the raw pixel data of the map as a single vector of `float` values, scanning the map horizontally from left to right and vertically from bottom to top (Cartesian coordinates); this is the `mapValues` variable that we prepared above.

The last two parameters here are optional, and are for SLiMgui's benefit. The first parameter, `valueRange`, gives the permissible range of values for the map data; this need not match the actual range of the data. The purpose of this is to tell SLiMgui what value range should be displayed using distinct colors; values outside this range will be clamped to be within the range for display. The second parameter, `colors`, gives a vector of color strings that specify how particular values should be displayed (see the Eidos manual for details on color strings). The lowest value in `valueRange` will be displayed using the first color in `colors`; the highest value in `valueRange` will be displayed using the last color in `colors`. Color values in between will be evenly distributed across `valueRange`, and intermediate values – those not corresponding exactly to a given color – will be displayed using an interpolation between the two nearest color values. Here, the values supplied for these parameters indicate that a value of `0.0` should be displayed with the color `"#0000CC"` (a dark blue), whereas a value of `1.0` should use color `"#55FF22"` (a medium green). Values between `0.0` and `1.0` would use an interpolation between those shades, but in fact our map data is binary, so that does not arise.

With that, we have defined a spatial map and told SLiMgui how to display it. We now just need to use it to govern the model dynamics. At the end of the `1 late()` event the positions of all individuals are initialized to be near a particular spot in East Africa, using `rnorm()` to draw the coordinates instead of using the `pointUniform()` method we have used in previous recipes. Then in our `modifyChild()` callback we enforce that individuals can only disperse to land:

```
modifyChild() {
    do pos = parent1.spatialPosition + rnorm(2, 0, 2.0);
    while (!p1.pointInBounds(pos));

    // prevent dispersal into water
    if (p1.spatialMapValue("world", pos) == 0.0)
       return F;

    child.setSpatialPosition(pos);
    return T;
}
```

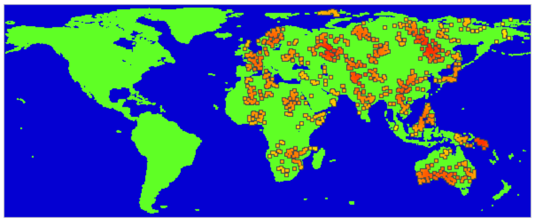
The first couple of lines generate a random offspring position based upon the position of the first parent, as we have seen in previous recipes. That code loops until a point inside the spatial bounds of the subpopulation in generated. Next, the callback consults the spatial map to find out the value at the candidate point using the `spatialMapValue()` method, giving it the name of the map and the candidate point. This method simply looks up the value nearest to the given point in the map data. If it is `0.0` – the value we used for water – then the callback returns `F`, rejecting the proposed child. Otherwise, the location is on land, so it is set as the new child's position and `T` is returned to accept the proposed child.

Notice, then, that a reprising boundary condition is used for the edges of the map, but an absorbing boundary condition is used for the coastlines. This means that individuals close to a coastline suffer a fitness penalty; their children are relatively likely to land in water, and when they do, they don't get another chance to generate a different child location. This is part of the reason that colonizing areas like Indonesia is difficult in this model (that fact that locations in places like

Indonesia are relatively unlikely to be chosen as child locations in the first place is also important). We can change the modifyChild() callback's code a bit to change that:

```
modifyChild() {
    do {
       do pos = parent1.spatialPosition + rnorm(2, 0, 2.0);
       while (!p1.pointInBounds(pos));
    } while (p1.spatialMapValue("world", pos) == 0.0);

    child.setSpatialPosition(pos);
    return T;
}
```

Now the boundary condition on coastlines is reprising also, and a quick run of the model shows that that allows much more dispersal into small land areas:



Indonesia and Australia are soon reached, and the UK and Madagascar often also support populations. Reaching North America is still quite difficult, however.

This is obviously just a fun toy model, but it would be easy to extend. A map using more values, to indicate things like mountain ranges, could be used, and the map could be much higher resolution (SLiM places no limit on the size of spatial maps, as long as your computer has enough memory). Dispersal on a high-resolution map could be much more short-range, making it so that even small barriers like rivers would present obstacles to dispersal. A much larger population size would probably be appropriate, for most organisms. Moreover, instead of using a constant population size as this model does, which is clearly unrealistic, the population size could be related to fitness in such a way that when the population discovers a new area and expands into it, thereby increasing in fitness since the effects of competition are diminished, the population size would increase to reflect the new higher carrying capacity; this might fall out naturally in a nonWF model (see section 15.10), but would have to be implemented in a WF model such as the one shown here. Mate choice could be based not only on spatial distance, but also upon, for example, the map value at a point intermediate between the two proposed parents, so that a mountain range would produce vicariance between even closely adjacent subpopulations. All of these sorts of features could be added with just a few more lines of code. Note also that although this model reads its spatial map in from a text file, it is also straightforward to construct a map programmatically, at runtime; see `twoHabitatMap.txt` in the online SLiM-Extras repository.

One particularly interesting feature for a biogeographic model like this would be to include spatial heterogeneity that affects the selection on individuals, such that there is selection pressure towards local adaptation. For instance, with this world map the more polar regions might exert selection toward more cold-adapted phenotypes whereas the more tropical regions might select for more warm-adapted phenotypes. In section 14.9 we saw a very primitive stab at this sort of model, with the introduction of a simple linear environmental gradient. Real landscapes are more complicated than that, though – mountaintops are similar to polar environments, whereas coastlines tend to have more moderate climates, for example. In the next section, we'll look at a model of adaptation to spatial heterogeneity that goes beyond a simple linear environmental gradient by using a spatial map.

14.11 Local adaptation on a heterogeneous landscape map

The previous section introduced the ability to define an arbitrary landscape map, whereas in section 14.9 we explored a model of adaptation to a linear environmental gradient. Let's try combining those two approaches, to see how complex environmental heterogeneity influences evolutionary outcomes like divergence and speciation. This recipe will demonstrate such an approach, inspired by the model of Haller, Mazzucco & Dieckmann (2013), although the landscapes generated here will be fairly different from those used in that paper. This recipe will generate a random "landscape map" representing the local phenotypic optimum across the landscape, and will then simulate the local adaptation of spatial groups to the conditions of that landscape. Here the landscape is generated algorithmically, but it would be trivial to instead read a landscape map from a file as was done in the previous recipe.

The model of section 14.9 provides us with a quantitative trait based upon underlying randomly arising QTLs, with phenotypic competition and assortative mating based upon that quantitative trait. Let's assume that machinery for now (the full recipe will be presented at the end), and look at the parts that are new. Most importantly, we have gotten rid of the slope constant of section 14.9, and instead here generate a heterogeneous landscape:

```
1 late() {
    sim.addSubpop("p1", N);

    p1.setSpatialBounds(c(0.0, 0.0, 0.0, 1.0, 1.0, 1.0));

    defineConstant("mapValues", runif(25, 0, 1));
    p1.defineSpatialMap("map1", "xy", c(5, 5), mapValues, interpolate=T,
      valueRange=c(0.0, 1.0), colors=c("red", "yellow"));

    for (ind in p1.individuals)
      ind.setSpatialPosition(p1.pointUniform());
    p1.individuals.z = 0.0;
}
```

We define spatial bounds of `[0, 1]` for each dimension, including the *z* dimension that is used for phenotype. A map is then generated simply as a set of 25 draws from a uniform distribution between `0` and `1`. This map, saved off in the defined constant mapValues (we will use it later), is set as a spatial map on subpopulation `p1` with a call to `defineSpatialMap()`. We specify that it corresponds to dimensions `"xy"`, that it is based on a 5x5 pixel grid (thus the 25 values), that values are expected to range between `0.0` and `1.0`, and that colors for that range should range from red to yellow.

We'll look at what this ends up looking like in a moment, but first let's finish building the model. In the `1: late()` event, we will replace the code from section 14.9 that colors individuals according to phenotype with new code that uses the same color scheme as the landscape coloring:

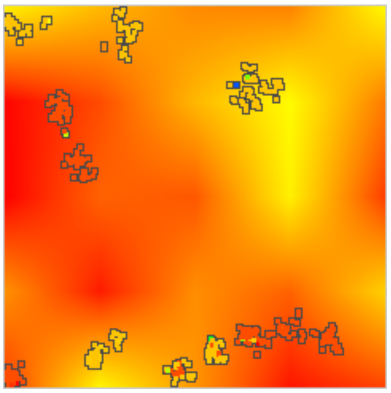
```
// color individuals according to phenotype
inds.color = p1.spatialMapColor("map1", phenotype);
```

This uses the `spatialMapColor()` method of `Subpopulation`, which translates a value into a color using the mapping established by a particular spatial map. In this way, the colors of individuals adapted to a given phenotypic optimum will exactly match the colors of map areas where that phenotypic optimum exists. Individuals that are perfectly adapted to their environment will therefore be displayed in SLiMgui in a color that matches their environment, whereas a mismatch in color between an individual and its environment will indicate maladaptation.

Finally, the global `fitness()` callback needs to change to use `spatialMapValue()` to find the phenotypic optimum for the point in space occupied by the focal individual. The map is looked up by name, as we saw in the previous section, and the location of the focal individual is obtained using its `spatialPosition()` method. We select just the *x* and *y* coordinates of the location, since those are the dimensions used by the spatial map. The final callback looks like this:

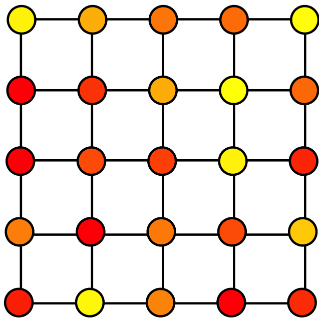
```
fitness(NULL) {    // reward proximity to the optimum
    location = individual.spatialPosition[0:1];
    optimum = subpop.spatialMapValue("map1", location);
    return 1.0 + dnorm(optimum - individual.z, mean=0.0, sd=sigma_K);
}
```

The rest of the recipe is as it was before. When we run the model, here's an example of what we see:

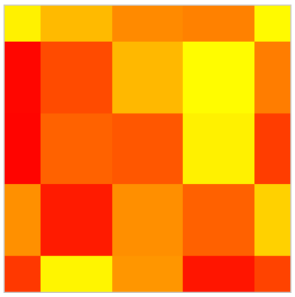


We have a nice randomly heterogeneous landscape, and the population has clearly adapted to it; we have reddish individuals in two of the more reddish areas, and orange individuals in three more orange areas. As before, the structure of neutral diversity visible in the chromosome view provides clear evidence of reproductive isolation and speciation.

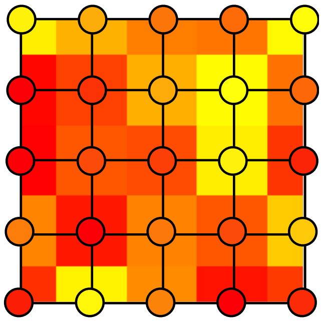
There is one thing that may be surprising, however. We supplied a `5x5` map to `defineSpatialMap()`, but the snapshot above shows what appears to be a continuous landscape. This is a result of the `interpolation=T` parameter we supplied to `defineSpatialMap()`, which instructed it to use interpolation (bilinear interpolation, in this case, to be precise) to make the landscape continuous. To understand better how that works, let's look in a little more detail at how SLiM builds landscape maps. First of all, here is the `5x5` grid of values that we supplied to `defineSpatialMap()`, colored according to the given color map:



Given this particular pixel grid, if we were to supply `interpolate=F` to `defineSpatialMap()` instead, the landscape displayed by SLiMgui would look like this:

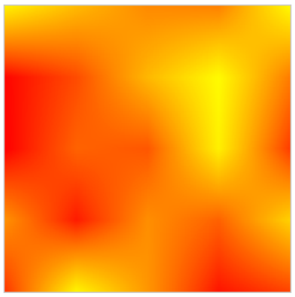


Note that because the pixel grid is aligned with the corners of the spatial bounds of the subpopulation, only ½ or ¼ of the area of the outer pixels is contained within bounds. The reason for this is clear if we look at the pixel grid superimposed on that landscape:

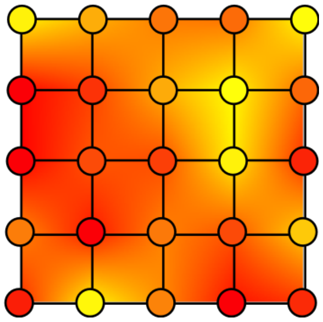


This is by design; it is the most natural way to handle such spatial maps when interpolation is involved (try thinking through the alternative to see why), and for consistency it is also how SLiM handles spatial maps when interpolation is not used.

So now when interpolation is turned on, the landscape looks like this:



This is the result of bilinear interpolation, which shades continuously between the defined points to produce a continuous map. The values defined by the pixel grid remain fixed, however. To illustrate that, here is the pixel grid superimposed on the interpolated landscape:

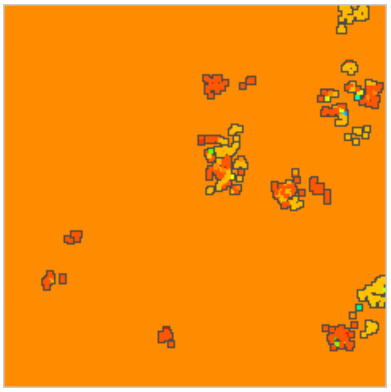


SLiM does not interpolate statically; it does not generate and store an interpolated map of some large but fixed size. Instead, when interpolation is enabled for a given spatial map, it calculates the exact interpolated value for a given point upon request. Interpolated maps are therefore completely continuous and effectively infinite-resolution (within the precision limits of floating-point numbers). With only 25 defined values, we therefore have an infinitely detailed landscape. In the previous recipe, using the world map, we did not enable interpolation, because we actually wanted the pixel grid; we wanted a world of binary pixels, either land or water, without allowing any shading between the two.

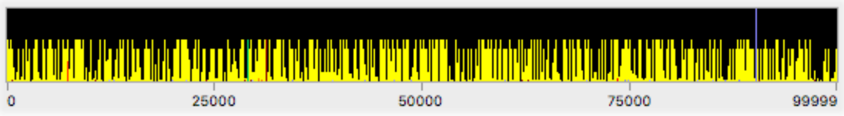
A logical step following the work of Haller, Mazzucco & Dieckmann (2013) would be to introduce temporal change in the landscape as well. We will not delve into that idea in any detail; but it is worth noting that that, too, is quite easy in SLiM. This is not part of the official recipe for this section – but try adding this code:

```
1: late()
{
    weight = (cos((sim.generation - 1) / 1000.0) + 1.0) / 2.0;
    newMap = weight * mapValues + (1 - weight) * 0.5;
    p1.defineSpatialMap("map1", "xy", c(5, 5), newMap, interpolate=T,
      valueRange=c(0.0, 1.0), colors=c("red", "yellow"));
}
```

This will cause the landscape to slowly cycle between heterogeneity and homogeneity. During the heterogeneous phases, speciation generally occurs as seen above. As the landscape fades into homogeneity, these species can persist, preserved by assortative mating and by the negative frequency-dependence of the competition function, such that speciation continues even when the landscape heterogeneity is completely gone:



Although the two species appear to have become sympatric in some areas, considerable reproductive isolation remains:



And when the heterogeneity returns to the landscape, the species can find their way back to areas where they are well-adapted – albeit with some evidence of genetic intermingling with the other species, such as some partially introgressed haplotypes. There is probably a lot of interesting work to be done on these sorts of temporal dynamics.

In any case, here is the full model (without the temporal-change code discussed just above), for posterity:

```
initialize() {
    defineConstant("sigma_C", 0.1);
    defineConstant("sigma_K", 0.5);
    defineConstant("sigma_M", 0.1);
    defineConstant("N", 500);

    initializeSLiMOptions(dimensionality="xyz");
    initializeMutationRate(1e-6);
    initializeMutationType("m1", 0.5, "f", 0.0);        // neutral
    initializeMutationType("m2", 0.5, "n", 0.0, 1.0);   // QTL
    m2.convertToSubstitution = F;

    initializeGenomicElementType("g1", c(m1, m2), c(1, 0.1));
    initializeGenomicElement(g1, 0, 1e5 - 1);
    initializeRecombinationRate(1e-8);

    initializeInteractionType(1, "xyz", reciprocal=T,
      maxDistance=sigma_C * 3);     // competition
    i1.setInteractionFunction("n", 1.0, sigma_C);
    initializeInteractionType(2, "xyz", reciprocal=T,
      maxDistance=sigma_M * 3);     // mate choice
    i2.setInteractionFunction("n", 1.0, sigma_M);
}
1 late() {
    sim.addSubpop("p1", N);
    p1.setSpatialBounds(c(0.0, 0.0, 0.0, 1.0, 1.0, 1.0));

    defineConstant("mapValues", runif(25, 0, 1));
    p1.defineSpatialMap("map1", "xy", c(5, 5), mapValues, interpolate=T,
      valueRange=c(0.0, 1.0), colors=c("red", "yellow"));

    for (ind in p1.individuals)
      ind.setSpatialPosition(p1.pointUniform());
    p1.individuals.z = 0.0;
}
modifyChild() {
    // set offspring position based on parental position
    do
      pos = c(parent1.spatialPosition[0:1] + rnorm(2, 0, 0.005), 0.0);
    while (!p1.pointInBounds(pos));
    child.setSpatialPosition(pos);

    return T;
}
1: late() {
    // construct phenotypes from the additive effects of QTLs
    inds = sim.subpopulations.individuals;
    phenotype = inds.sumOfMutationsOfType(m2);
    inds.z = phenotype;

    // color individuals according to phenotype
    inds.color = p1.spatialMapColor("map1", phenotype);

    // evaluate interactions
    i1.evaluate();
    i2.evaluate();
}
```

```
fitness(m2) {      // make QTLs intrinsically neutral
    return 1.0;
}
fitness(NULL) {    // reward proximity to the optimum
    location = individual.spatialPosition[0:1];
    optimum = subpop.spatialMapValue("map1", location);
    return 1.0 + dnorm(optimum - individual.z, mean=0.0, sd=sigma_K);
}
fitness(NULL) {    // phenotypic competition
    totalStrength = sum(i1.strength(individual));
    return 1.0 - totalStrength / p1.individualCount;
}
mateChoice() {
    // spatial mate choice
    return i2.strength(individual);
}
10000 late() {
    sim.simulationFinished();
}
```

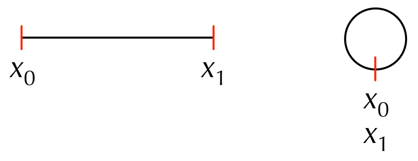
This is the most complex recipe we will build involving spatiality, interactions, and landscape maps, but there is so much more that could be done. Interactions could be based upon genetics in ways beyond the QTL-based models we have explored; a spatial green-beard model would be interesting, for example. SLiM allows multiple landscape maps to be defined; it would be interesting to bring in empirical data on elevation, rainfall, mean temperature, and a host of other variables, and allow a population to evolve in a complex, multidimensional landscape to see whether realistic patterns of spatial biodiversity might be realized. One could even create a model in which the behavior of the organisms on the landscape modify the landscape itself – a model of desertification driven by overgrazing, for example.

Before we wrap up our discussion of spatial models, however, there is one remaining topic that we deferred.

14.12 Periodic spatial boundaries

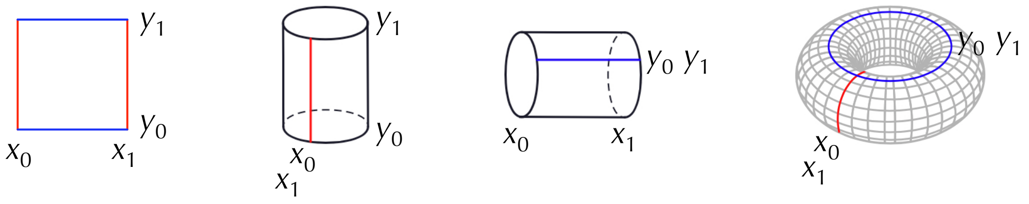
In section 14.3, various options for spatial boundary conditions were introduced: stopping, absorbing, reflecting, and reprising boundaries. The possibility of periodic spatial boundaries was also mentioned, but was deferred as an advanced topic. The time has come to explore this concept.

A periodic spatial boundary is one which wraps around: one edge of a spatial dimension is connected seamlessly to the opposite edge. A non-periodic one-dimensional bounded space is a line segment: points in this space may fall anywhere between x_0 and x_1. An individual might travel from x_0 to x_1, at which point the end of the line segment is reached and motion must stop or reverse. The periodic version of this is a circle: x_0 and x_1 have been joined together to form a closed curve:



Here, an individual might travel from x_0 to x_1 and continue onwards; at the moment it reaches x_1 it has also, simultaneously, returned to x_0, and may continue towards x_1 again (and again, and again). Note that there is no "seam" and no "privileged point" in this space; the spatial topology at every point is identical.

A non-periodic two-dimensional bounded space is a rectangle with extents [x_0, x_1] and [y_0, y_1]. There are three periodic versions of this: x_0 and x_1 may be joined, y_0 and y_1 may be joined, or both pairs may be joined. The first two options produce a topology like the surface of a cylinder without end caps; the third option produces not a sphere (as one might guess), but a torus, like the surface of a doughnut:



Again, movement along the periodic dimension(s) may continue indefinitely, wrapping around at the boundary; and again, there is no "seam" or "privileged point" in these spaces (along the periodic axis or axes).

Finally, a non-periodic three-dimensional bounded space is a cube; it may be made periodic in *x*, *y*, *z*, *x* and *y*, *x* and *z*, *y* and *z*, or *x* and *y* and *z*, yielding seven different periodic versions of three-dimensional space. The topology of these is harder to visualize, but the principle is the same: movement along the periodic axis or axes may continue indefinitely because it wraps around, and along the periodic axis or axes there is no "seam".

This is all rather abstract, but periodic boundary conditions are very useful in modeling, especially when doing theoretical work rather than trying to simulate a real landscape. The reason is simple: periodic spatial boundaries eliminate edge effects, which are otherwise a source of bias in spatial models. In effect, periodic boundaries allow you to model an infinite space with no edges at all. Of course the space is not really infinite, but instead repeats periodically; but if the spatial scale of important interactions and dynamics in the model is small compared to the size of the periodic space, this is often an acceptable approximation.

Setting up periodic spatial boundaries in SLiM is a little bit more complex than implementing other boundary conditions. The reason is that periodic spatial boundaries fundamentally change many aspects of SLiM's spatial engine; enforcing the boundary condition is no longer just a question of modifying generated offspring positions in a particular way (although that is one part of it). For instance, consider two individuals that occupy positions (0.0, 0.1) and (0.0, 0.9) in a two-dimensional space with extent [0.0, 1.0] in both *x* and *y*. With any other boundary condition, the distance between these two individuals is 0.8 (0.9 – 0.1). With periodic boundaries, however, the distance between them is 0.2, because a line of length 0.2 may be drawn between them that wraps around the boundary in the *y* dimension. By definition, the distance between two points in a periodic space is always the *shortest* distance possible out of the infinitely many different distances that could be calculated. This means that distances, interaction strengths, and indeed all of the underlying mechanics of `InteractionType`'s spatial queries must take the periodicity of the space into account.

For this reason, periodic spatial boundaries must be declared up front, and cannot be changed subsequently. This declaration is done with a parameter to `initializeSLiMOptions()` named `periodicity`, which specifies the periodic spatial dimensions as a `string`. In this recipe, we will work with a two-dimensional model that is periodic in both dimensions – a toroidal model, as pictured above. This can be set up as follows:

```
initialize() {
    initializeSLiMOptions(dimensionality="xy", periodicity="xy");
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
    initializeInteractionType("i1", "xy", reciprocal=T, maxDistance=0.2);
    i1.setInteractionFunction("n", 1.0, 0.1);
}
```

The `initializeSLiMOptions()` call establishes a 2-D space (with `dimensionality="xy"`) and then declares both of those dimensions to be periodic (with `periodicity="xy"`). We also set up a spatial interaction here, involving both spatial dimensions; it uses a Gaussian interaction function with a standard deviation of `0.1`, so it falls off at well under the spatial scale of the model as a whole. We declare it to have a maximum distance of `0.2`, for efficiency; the interaction strength will be very low further than two standard deviations out anyway.

Next, let's set up a subpopulation with random initial positions:

```
1 late() {
    sim.addSubpop("p1", 2000);
    p1.individuals.x = runif(p1.individualCount);
    p1.individuals.y = runif(p1.individualCount);
}
```

Nothing surprising here. Let's implement a `modifyChild()` callback to set up offspring positions, very much as we did in the recipes in section 14.3:

```
modifyChild() {
    pos = parent1.spatialPosition + rnorm(2, 0, 0.02);
    child.setSpatialPosition(p1.pointPeriodic(pos));
    return T;
}
```

This uses a function named `pointPeriodic()` that is similar to the `pointStopped()` and `pointReflected()` functions we saw before; it translates the point it is passed so that it falls within the spatial boundaries, while implementing the periodic boundary conditions requested. In this case, `pointPeriodic()` wraps a point that lies beyond the periodic spatial boundaries, just as if the offspring had walked off of one edge of the space and re-appeared at the opposite edge.

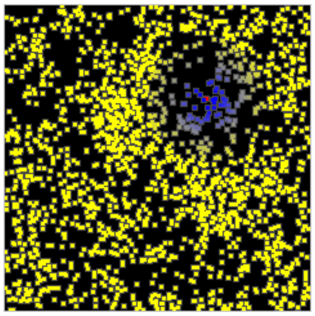
We need an event to define the end of the simulation, as usual:

```
1000 late() { sim.outputFixedMutations(); }
```

And now let's do something a bit more interesting: let's use the interaction type that we defined above to show, visually in SLiMgui, how interactions work in periodic space:

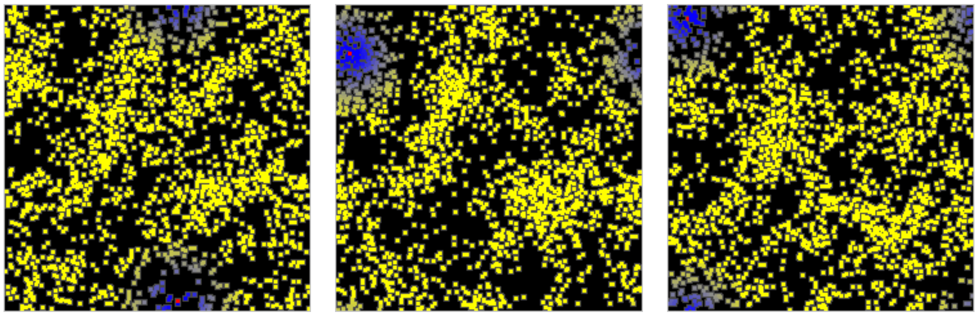
```
late()
{
    i1.evaluate();
    focus = sample(p1.individuals, 1);
    s = i1.strength(focus);
    inds = p1.individuals;
    for (i in seqAlong(s))
       inds[i].color = rgb2color(c(1.0 - s[i], 1.0 - s[i], s[i]));
    focus.color = "red";
}
```

This `late()` event runs in every generation. It evaluates the interaction, then chooses a focal individual randomly from the population. It asks the interaction type to calculate the interaction strength between the focal individual and all other individuals; then it loops over the individuals (by index) and sets each one's color in SLiMgui using a particular formula (see the Eidos manual for discussion of the `rgb2color()` function). Finally, it sets the color of the focal individual itself to red. When this model is run, a typical generation looks like this:



The focal individual can be seen in red. The individuals closest to it are blue, while those farthest away are yellow. Because of the particular RGB (red, green, blue) color values passed to `rgb2color()`, the color of individuals at intermediate distances fades smoothly from blue to yellow. This is a nice illustration of the shape of the interaction kernel, and in fact this sort of coloration strategy can be quite useful in testing and visualizing spatial models.

The snapshot above, however, involved a focal individual that was far from any of the spatial boundaries. When a different focal individual is chosen, we can see that the spatial interaction wraps around the edges of the periodic space:



The third snapshot illustrates that wrapping occurs in both spatial dimensions, not just one at a time. Due to the toroidal geometry of the space, the four corners of the space as displayed in SLiMgui are actually all the same point! In the diagram above of the toroidal geometry of this space, the four corners as displayed in SLiMgui correspond to the intersection of the blue and red lines drawn on the torus. Note that topologically, there is nothing special about the blue and red lines in particular; every point on the torus lies at the intersection between a curve that circles around the major circumference of the torus (like the blue line) and a curve that circles around the minor circumference of the torus (like the red line). An individual living in this space cannot tell whether it is at the periodic boundary or not; as was emphasized earlier, there is no seam.

If you wish, you can play with this model by making only the *x* dimension periodic, or only the *y* dimension, to see how that affects the spatial interaction and what the resulting cylindrical topology feels like in practice. If you do so, note that `pointPeriodic()` will enforce only the periodic boundary condition; it will leave coordinates that are not periodic unmodified. To keep the modeled individuals inside bounds, some boundary condition – whether stopping, reflecting, absorbing, or reprising – must be enforced for the non-periodic coordinates. This can be done just as it was in section 14.3; in particular, it is useful to note that a call to `pointPeriodic()` can be wrapped inside a call to `pointStopped()` or `pointReflected()` to achieve the desired effect. This works because `pointPeriodic()` has already brought the periodic coordinates into bounds, so they will not be modified by `pointStopped()` or `pointReflected()`. So a model that used periodic boundaries for only one of the two axes, and that enforced reflecting boundaries on the non-periodic axis, could use a `modifyChild()` callback like this:

```
modifyChild() {
    pos = parent1.spatialPosition + rnorm(2, 0, 0.02);
    child.setSpatialPosition(p1.pointReflected(p1.pointPeriodic(pos)));
    return T;
}
```

All of the other elements of spatial modeling that were introduced in earlier recipes in this chapter – spatial competition, spatial mate choice, landscape maps – will work with periodic spatial boundaries. You can still model phenotype as a spatial dimension, too, as in section 14.7 for example; you will just (probably) not want that dimension to be periodic, since phenotypic traits are usually linear – being very short is not the same thing as being very tall!

The concept of periodic space can take some getting used to; cylindrical or toroidal space may seem rather artificial at first. But in fact, because of the absence of edge effects, periodic space is actually *less* artificial than other arbitrarily-chosen boundary conditions, in many ways; it will not exhibit biases in the spatial density of individuals in one part of the space versus another, individuals everywhere will feel the same average interaction strength if they are randomly distributed, and motion in particular directions from particular locations will not be artificially impeded.

Because of the greater underlying complexity, models using periodic space will be a little slower in SLiM than non-periodic models, but unless population size is large the difference in performance should be slight. Unless you actually *want* a particular edge effect in your model, perhaps reflecting some real-world landscape's dynamics, periodic boundaries may be the best option.

15. Going beyond Wright-Fisher models: nonWF model recipes

Beginning with SLiM 3.0, two fairly different types of models are supported in SLiM: Wright-Fisher or WF models, and non-Wright-Fisher or nonWF models. See section 1.6 for a discussion of the differences between these two types of models. All of the recipes presented so far have been WF models, since that is the default model type in SLiM. In this chapter, we will go beyond the assumptions and constraints of Wright-Fisher models, and will examine recipes for a variety of nonWF models.

A great deal of the overall design of SLiM is shared between WF and nonWF models. All of the Eidos classes that embody SLiM are the same (`SLiMSim`, `Subpopulation`, `Individual`, etc.), and the way that SLiM models the chromosome, genomes, mutations, and so forth is unchanged. Since that foundation is all shared, a good understanding of the concepts in the preceding chapters will be assumed. Many of the techniques presented in the preceding recipes will also work in nonWF models. We will not re-cast all of those techniques in a nonWF context, since that would mostly just be repetitive and uninteresting; instead, we will focus on the important ways in which nonWF models are different from WF models.

As discussed in more detail in section 1.6, the main differences between WF and nonWF models fall into a few major categories. First of all, in nonWF models generations may be overlapping and individuals can live for more than one generation; for this reason, in nonWF models the model's script is responsible for creating new offspring as needed, rather than that happening automatically every generation as in WF models. Second, for the same reason, in nonWF models the parental generation does not die off automatically after offspring are generated; instead, fitness governs mortality (rather than governing mating success as in WF models). Third – as a consequence of the previous two differences, really – in nonWF models population regulation is a consequence of the balance between individual reproduction and individual mortality, just as it is in natural populations, rather than being enforced through a set population size as in WF models. Fourth, migration in nonWF models is similarly managed on an individual basis in the model's script, rather than being done automatically by the SLiM engine based upon set migration rates.

All of this points to two basic observations. One observation is that the generation cycle is quite different between WF and nonWF models. Chapter 19 discusses the generation cycle for WF models, whereas chapter 20 discusses the generation cycle for nonWF models and the important conceptual ways in which it differs from the WF generation cycle. An understanding of those differences, such as the way in which the semantics of `early()` and `late()` events have changed and the way that the meaning of fitness has shifted, will be important to understand the recipes that follow, so chapter 20 should be consulted for further information as needed. The other observation is that nonWF models are generally more individual-based and more complex than WF models, because more responsibilities like offspring generation and migration have been pushed from SLiM onto the model's script. With this additional complexity comes considerable additional power and flexibility, however, as we will see.

15.1 A minimal nonWF model

Let's begin with a minimal nonWF model, similar to the minimal WF model presented in section 4.1. This will illustrate several of the fundamentals of nonWF models: how to switch SLiM into nonWF "mode", how to implement individual-based reproduction and density-dependent population regulation, and how to work with non-overlapping generations.

With no further ado, here is the recipe:

```
initialize() {
    initializeSLiMModelType("nonWF");
    defineConstant("K", 500);

    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;

    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);
}
reproduction() {
    subpop.addCrossed(individual, subpop.sampleIndividuals(1));
}
1 early() {
    sim.addSubpop("p1", 10);
}
early() {
    p1.fitnessScaling = K / p1.individualCount;
}
late() {
    inds = p1.individuals;
    catn(sim.generation + ": " + size(inds) + " (" + max(inds.age) + ")");
}
2000 late() {
    sim.outputFull(ages=T);
}
```

The first line of the `initialize()` callback is a call to `initializeSLiMModelType("nonWF")`; this tells SLiM that we are building a nonWF model. That has various consequences; it activates the nonWF generation cycle shown in chapter 20, for example, and it enables some properties and methods on SLiM's objects while disabling others. It is possible, when writing a WF model, to include a call to `initializeSLiMModelType("WF")`, but unnecessary, since that is the default.

The next line sets up a defined constant, `K`. This will be the carrying capacity for the model's population regulation; we'll cover that below.

The rest of the `initialize()` callback is much as we have seen before, but you might notice one surprising thing: we set the `convertToSubstitution` property of mutation type `m1` to `T`. In WF models, mutations convert to substitutions automatically; the default value of that property is `T`, so it would be redundant to set it to `T` again. In nonWF models, however, mutations do not convert to substitutions automatically; the `convertToSubstitution` property is `F` by default and must be set to `T` when desired. The reason is that in nonWF models fitness is absolute, not relative, and so only completely neutral mutations with no side effects are safe to convert to `Substitution` objects (see section 20.4 for further discussion). Since `m1` mutations are completely neutral in this model, we tell SLiM to allow them to fix; this will make the model run much faster.

The next script block is a new type of callback, a `reproduction()` callback, that may be used only in nonWF models. Such `reproduction()` callbacks are called once per individual, at the beginning of each generation; this provides an opportunity for that focal individual to generate offspring (which it might or might not do); see section 20.1 for further discussion. This callback calls `p1.sampleIndividuals(1)` to draw one random individual from `p1` as a mate, and then calls `subpop.addCrossed()` to add a new offspring individual that is the result of crossing – biparental sexual reproduction – between the focal individual for the callback (`individual`) and the chosen mate. The new individual is created, and is in fact returned to the caller, but is not actually added to the subpopulation until offspring generation is finished. Note that although each individual will generate exactly one offspring of its own here, as the focal individual or "first parent", it might also be chosen as a mate by another individual (perhaps more than once, or perhaps not at all).

The next script block returns us to more familiar territory, since it simply calls `addSubpop()` to create subpopulation `p1` with ten initial individuals. The only point to be made here is that while in a WF model this would set the subpopulation's size forever (until `setSubpopulationSize()` was called, at least), in a nonWF model this only sets the initial subpopulation size; the size of the subpopulation will henceforth be governed by birth and death events, not by the initial size set for it.

Speaking of death, the next `early()` event governs that. It calculates an absolute fitness value, `K / p1.individualCount`, and sets that into the `fitnessScaling` property of `p1`. We haven't seen this property before; in effect, it scales the absolute fitness of the subpopulation, because the calculated fitness for every individual in `p1` is multiplied by this value. It is essentially the same as writing a global `fitness(NULL)` callback that returns the same constant value for every individual, but it is much faster than that model design would be, since the `fitness(NULL)` callback would have to actually be called for every individual in every generation.

This `fitnessScaling` property may be used in WF models too, in fact, but is not generally useful in that context; since WF models use relative fitness, scaling the fitness of all individuals by the same constant has no effect. In nonWF models, however, it has a very important effect! This `fitnessScaling` factor is what regulates the population size in the model; if this line were commented out, the population would grow exponentially forever (until SLiM crashed, or got so slow as to be effectively halted). Instead, when the subpopulation size is less than `K`, `fitnessScaling` will be greater than `1.0` (and so no mortality will occur and the subpopulation size will grow); but if it is larger than `K`, `fitnessScaling` will be less than `1.0` and mortality will bring it back toward `K`. Since new individuals get generated at the beginning of each generation by our `reproduction()` callback, once the model reaches equilibrium the population size will double during offspring generation to around `1000`, then a `fitnessScaling` value of approximately `0.5` will be set, and then approximately half of the individuals will die during the survival life cycle stage, bringing the population size down to approximately `500` (i.e., `K`).

Note that there is nothing magical about this particular formula; any formula or model design that influences individual fitness in such a manner as to regulate the population size will work. This particular formula produces logistic growth until `K` is reached, and then stochastic population size fluctuation around `K` thenceforth. The population size will be stochastic around `K` because in nonWF models fitness is the probability of death, but of course sometimes more individuals will die than expected, sometimes less; the fate of each individual is in the hands of SLiM's random number generator.

Next we have a `late()` event that outputs two pieces of information in each generation: the population size, and the age of the oldest individual. Here's the initial output from one run:

```
1: 10 (0)
2: 20 (1)
3: 40 (2)
4: 80 (3)
5: 160 (4)
6: 320 (5)
7: 496 (6)
8: 485 (7)
9: 500 (6)
10: 522 (7)
...
```

You can see the exponential growth at the start settling in around 500 once the model reaches carrying capacity. You can also see that we already have overlapping generations in this model; the individuals at the end of generation 1 are of age 0 (newly generated juveniles), and that initial cohort ages without mortality during exponential growth (since we have not implemented a maximum age or any sort of age-dependent reduction in fitness). By generation 7, though, the carrying capacity has filled up and individuals start to die. Since every individual in this model has the same fitness, mortality is purely random, and sometimes you will get a Methuselah that lives to be 20 or even older; but most individuals will die through sheer bad luck before then, and the maximum age in this model will tend to fluctuate around 10 or 15. Later recipes will explore how to control the population age in biologically realistic ways, but for now let's just bask in the glory of the fact that we have already modeled something that can't be modeled in WF SLiM: overlapping generations.

The final event produces output from the model with `outputFull()`, as we have seen many times before. The only new element is the `ages=T` parameter, which requests that age information be added to the output (the details of the output format are given in section 23.1.1).

That's it; that completes our first nonWF recipe! In subsequent sections we will explore the greater power the nonWF paradigm affords us, because we can now control the mating, fecundity, migration, fitness, and survival of each individual.

15.2 Age structure (a life table model)

In the previous recipe, the probability of survival was the same regardless of age, and that produced a particular emergent age structure in the population. In most biological systems, however, the probability of survival is age-dependent. Commonly, this is modeled with a life table that gives the probability that an individual of a given age will die within the next time period (the next year, often).

To model non-overlapping generations in a nonWF model (as is always the case in WF models), one might use a life table that gives a probability of survival of 0.0 for all individuals of age 1 or older (newly generated juveniles having an age of 0); with such a life table, offspring would be generated and then the parental individuals (all having an age of 1) would all immediately die. In this model we will implement a slightly more complex life table, for an imaginary species that has high juvenile mortality, low adult mortality, and a maximum age of seven generations. We will also implement age-dependent fertility and density-dependent population regulation.

Let's look at this model one piece at a time, beginning with initialization:

```
initialize() {
    initializeSLiMModelType("nonWF");
    defineConstant("K", 30);
    defineConstant("L", c(0.7, 0.0, 0.0, 0.0, 0.25, 0.5, 0.75, 1.0));

    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;

    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);
}
```

This is identical to the previous recipe except for the addition of the defined constant L, which is our life table. It gives the probability of mortality for each age; newly generated juveniles have a mortality of 0.7 (i.e., 70%), then the mortality drops to zero for several years, and then it ramps gradually upward with increasing age until it reaches `1.0` for age `7`; all individuals of age `7` will die. Note that this is only the *age-related* mortality; density-dependence will also cause mortality, as we will see below, but that will be additional to this age-related mortality, which would occur even in a population that was not limited by its density.

Next, let's implement reproduction:

```
reproduction() {
    if (individual.age > 2)
       subpop.addCrossed(individual, subpop.sampleIndividuals(1));
}
```

This is the same as the `reproduction()` callback in the previous recipe, except that here we have prevented reproduction by individuals of age `2` or below. One could similarly limit or prevent reproduction in a nonWF model based upon genetics, individual state, resource acquisition, mate compatibility, or any other factor.

Population initialization looks like this:

```
1 early() {
    sim.addSubpop("p1", 10);
    p1.individuals.age = rdunif(10, min=0, max=7);
}
```

We again start at a population size of `10` and allow the population to grow upward to the carrying capacity (only `30` in this model, to make reading the output of the model easier). Since `addSubpop()` sets the age of all new individuals to `0`, that would provide our model with a bit of an artificial start, and it might also present difficulties since juvenile mortality in this model is so high – sometimes the population might go extinct before it reaches reproductive age. We therefore draw random ages from a discrete uniform distribution from `0` to `7`. If one had empirical data about the age distribution in one's system, that might of course be an even better starting point.

And here we manage both age-related and density-dependent mortality:

```
early() {
    // life table based individual mortality
    inds = p1.individuals;
    ages = inds.age;
    mortality = L[ages];
    survival = 1 - mortality;
    inds.fitnessScaling = survival;

    // density-dependence, factoring in individual mortality
    p1.fitnessScaling = K / (p1.individualCount * mean(survival));
}
```

We calculate the age-related mortality by getting all of the individuals in `p1`, getting their ages, and then looking up those ages in `L` to get a vector of the mortality rates for the individuals. Survival rates are the opposite of mortality rates, so we subtract from `1`; if an individual has a mortality rate of `1` it has a survival rate of `0`, and *vice versa*. Finally, we set those survival rates into the `fitnessScaling` properties of the individuals. We saw the `fitnessScaling` property of `Subpopulation` in the previous recipe, where it scaled the fitness of all individuals in the subpopulation by the same constant factor. The `fitnessScaling` property of `Individual` has much the same effect, but on an individual basis; each individual can have a different `fitnessScaling` value, which is multiplied into that individual's calculated fitness. This is equivalent to implementing a `fitness(NULL)` callback that returns a survival-based fitness effect for the focal individual based upon that individual's age; but this way is much faster since it is done in a vectorized fashion without `fitness()` callbacks.

Next, the callback above calculates density-dependent mortality based upon `K` and the current population size, as before, but also factors in the mean survival rate in the population due to age-related mortality. Without that correction, the population would equilibrate around a lower size than `K`, because age-related mortality would occur *in addition to* the density-dependent mortality necessary to bring the population down to `K`. With the correction, the population size should fluctuate stochastically around `K`, as desired. One could of course get fancier, and come up with equations that made the probability of density-dependent mortality depend upon age (or any other individual state) in some manner; perhaps older individuals would be weaker and more vulnerable to diseases and parasites that are common when population density is high, for example.

```
late() {
    // print our age distribution after mortality
    catn(sim.generation + ": " + paste(sort(p1.individuals.age)));
}
2000 late() { sim.outputFixedMutations(); }
```

These are the last components of our model: output and termination. The `late()` output event prints the population's age distribution in each generation; this is post-mortality, since `late()` events run after the survivial/viability generation cycle stage in nonWF models. A typical run:

```
1: 0 0 1 1 3 3 3 6 6 6
2: 0 0 0 0 0 0 1 1 2 2 4 4 4
3: 0 0 0 0 0 1 1 1 1 1 1 2 2 3 3 5 5 5
4: 0 0 0 0 1 1 1 1 1 2 2 2 2 2 2 3 3 4 4 6 6 6
5: 0 0 0 0 1 1 1 1 2 2 2 2 2 3 3 3 3 3 3 4 4 5
...
1996: 0 0 0 0 0 0 1 1 1 1 1 1 1 1 2 2 2 2 3 3 3 4 4 4 4 4 5 6
1997: 0 0 0 0 0 0 0 1 1 1 1 1 1 2 2 2 2 2 2 2 2 3 3 3 3 4 4 4 5 5 5
1998: 0 0 0 0 1 1 1 1 1 1 2 2 2 2 2 2 3 3 3 3 3 3 3 3 4 4 4 4 5 5 6 6
1999: 0 0 0 0 1 1 1 1 2 2 2 2 2 2 2 3 3 3 3 3 4 4 4 4 5 5 5 5
2000: 0 0 0 0 0 0 0 1 1 1 1 2 2 2 2 3 3 3 3 3 3 4 4 5 6
```

The beginning of the output shows growth toward the carrying capacity; even before the carrying capacity is reached some age-related mortality occurs. The end of the output shows the (somewhat stochastic) equilibrium population size and age structure. With this life table, the population is dominated by middle-aged individuals; most juveniles die, and few individuals make it to age `7` since the mortality rate ramps upward beginning at age `4`. Note that no individuals of age `7` are visible here because this output is post-mortality; no individual of age `7` should ever exist at this point in the generation cycle. If this output event were an `early()` event instead, however, we would expect to see the occasional age `7` individual.

This model uses a life table, but the larger point is that nonWF models allow one to model any individual-based mortality effects, whether due to genetics (which would typically occur through SLiM's built-in fitness calculations), age (as with a life table or similar scheme), density (as also modeled here), individual state, environmental effects, or anything else. Fitness effects influencing survival can be expressed through `fitness()` callbacks, or using the `fitnessScaling` properties of `Subpopulation` and `Individual` that we used here.

15.3 Monogamous mating and variation in litter size

In the previous recipe we explored how to manipulate individual fitness values in order to implement age-dependent mortality using a life table. In this recipe we will look at the other end of the circle of life: mate choice and fertility. The previous nonWF models we have built have used an extremely simplistic model of reproduction in which each individual of reproductive age produces exactly one offspring per generation itself with a randomly selected mate (and may be chosen as a mate by another individual, too). Here we will implement a very different model of reproduction: monogamy (within a single breeding season), and generation of a litter of offspring of non-deterministic size.

This model will look very similar to section 15.1's recipe, so let's just see the whole model all at once:

```
initialize() {
    initializeSLiMModelType("nonWF");
    defineConstant("K", 500);

    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;

    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);
}
reproduction() {
    // randomize the order of p1.individuals
    parents = sample(p1.individuals, p1.individualCount);

    // draw monogamous pairs and generate litters
    for (i in seq(0, p1.individualCount - 2, by=2))
    {
       parent1 = parents[i];
       parent2 = parents[i + 1];
       litterSize = rpois(1, 2.3);

       for (j in seqLen(litterSize))
          p1.addCrossed(parent1, parent2);
    }

    // disable this callback for this generation
    self.active = 0;
}
1 early() {
    sim.addSubpop("p1", 10);
}
early() {
    p1.fitnessScaling = K / p1.individualCount;
}
late() {
    inds = p1.individuals;
    catn(sim.generation + ": " + size(inds) + " (" + max(inds.age) + ")");
}
2000 late() {
    sim.outputFull(ages=T);
}
```

This is, in fact, identical to section 15.1 except for the `reproduction()` callback, so let's look at that in detail:

```
reproduction() {
    // randomize the order of p1.individuals
    parents = sample(p1.individuals, p1.individualCount);

    // draw monogamous pairs and generate litters
    for (i in seq(0, p1.individualCount - 2, by=2))
    {
       parent1 = parents[i];
       parent2 = parents[i + 1];
       litterSize = rpois(1, 2.7);

       for (j in 1:litterSize)
          p1.addCrossed(parent1, parent2);
    }

    // disable this callback for this generation
    self.active = 0;
}
```

We do something quite different here: this `reproduction()` callback runs only once per generation, not once per individual! It disables itself at the end of its own execution by setting its active flag to `0` (see section 22.8 for discussion of this feature, which we haven't seen much before now). The `reproduction()` callback is called by SLiM for some particular focal individual, but it ignores that individual and instead generates offspring for all of the individuals in the whole population all at once. This is perfectly fine, and can be a useful strategy when the reproduction behavior of individuals is non-independent; with monogamy, for example, once two individuals have formed a mating pair those individuals are not available to be chosen as mates by any other individuals, so mating behavior in this model is non-independent.

The first thing we want to do is choose all of the monogamous mating pairs. The order of individuals in SLiM is not guaranteed to be random in SLiM, so it would be unwise to simply pair individuals `0` and `1`, `2` and `3`, etc.; that could lead to biases in mate choice that could manifest in strangely skewed genetics over time. Instead, we use the `sample()` function to draw a complete sample from the population, without replacement, effectively randomizing its order. Then we pair individuals `0` and `1`, `2` and `3`, etc., from *that*, which is safe. We do that pairing with a `for` loop over the even values up to `p1.individualCount - 2` (guaranteeing that a pair of individuals remains the last time through the loop, not just an odd one out at the end). Individuals `i` and `i+1` are then taken to be a monogamous mating pair. Of course one could implement any mating scheme at all; females could choose males assortatively, or based upon their physical condition, or in any other manner, and monogamy does not need to be enforced (as we saw in the previous two recipes).

Next, we want to generate a litter for that mating pair. We draw the size of the litter from a Poisson distribution with a mean of `2.7`, arbitrarily. At the risk of sounding like a broken record, of course litter size could depend upon anything at all – the genetics of the two parents, their genetic compatibility, their respective conditions, their ages, their fecundity the previous year, their phenotypic match with their environment, etc. Here, we happen to use a Poisson distribution with a mean of `2.7`. That gives us a litter size; we then generate the litter by calling `addCrossed()` that many times with the same parents.

The only thing left is for the `reproduction()` callback to deactivate itself, as explained above. This model has the same output code as section 15.1's recipe; a typical run produces:

```
...
1995: 497 (6)
1996: 531 (7)
1997: 524 (6)
1998: 497 (7)
1999: 529 (8)
2000: 511 (6)
```

Note that the equilibrium age here is around `6` to `7`, where in section 15.1 it was more around `10` to `15`. That is because section 15.1's recipe produced one offspring per individual per generation (not counting being chosen as a mate by another reproducing individual), whereas this recipes produces about `1.35` (half of `2.7`). That floods this model with young individuals, relative to the earlier model. Density-dependent mortality and carrying capacity remain the same, however, so skewing the age distribution towards juveniles in that manner inevitably means fewer old individuals and a shorter expected lifespan. That happens because with more offspring generated, the pre-mortality population size is larger, and so (given that the carrying capacity is the same) density-dependent selection is stronger, individual fitness is lower, and the probability of mortality per individual is higher, reducing the expected lifespan.

15.4 Beneficial mutations and absolute fitness

Thus far, we have only looked at neutral nonWF models. Fitness in nonWF models is absolute and affects survival, where in WF models it is relative and affects mating success; this makes fitness dynamics a bit different between nonWF and WF models. In particular, since one cannot survive with more than a 100% probability, fitness values above `1.0` in nonWF models do not benefit the individual at all; fitness values above `1.0` are interpreted as being `1.0`. However, fitness is also multiplicative (in both nonWF and WF models), and the important thing is the final fitness value for an individual. The way this works out in practice can be a bit counterintuitive, so in this section we will explore a simple model of an introduced beneficial mutation that sweeps to fixation in a population, and we will look at the population dynamics as it does so.

The recipe is again based on that of section 15.1:

```
initialize() {
    initializeSLiMModelType("nonWF");
    defineConstant("K", 500);

    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;
    initializeMutationType("m2", 1.0, "f", 0.5);   // dominant beneficial

    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);
}
reproduction() {
    for (i in 1:5)
       subpop.addCrossed(individual, subpop.sampleIndividuals(1));
}
1 early() {
    sim.addSubpop("p1", 10);
}
```

```
100 early() {
    mutant = sample(p1.individuals.genomes, 10);
    mutant.addNewDrawnMutation(m2, 10000);
}
early() {
    p1.fitnessScaling = K / p1.individualCount;
}
late() {
    inds = p1.individuals;
    catn(sim.generation + ": " + size(inds) + " (" + max(inds.age) + ")");
}
2000 late() {
    sim.outputFull(ages=T);
}
```

The changes from section 15.1 are minor. In the `initialize()` callback we create a mutation type `m2`, for beneficial mutations; this has quite a strong selection coefficient and is dominant, to make it less likely to be lost to drift at the very beginning, but that is unimportant to the point of this recipe; we just don't want to have to get into making the recipe conditional on fixation since that is an extra complication (see section 10.2). In the `reproduction()` callback each individual now reproduces five times per generation, creating very strong density-dependent selection; this is a highly fecund species. That is not essential to the point of this recipe, but it will make the effect more obvious. In a new `100 early()` event we now select one genome from the population at random, and add an `m2` mutation to it. The rest of the model is the same. The `m2` mutation will (usually) sweep to fixation, and we will look at the resulting population size and age structure.

At the beginning, the model rapidly grows to the carrying capacity and stays there (each output line, remember is a generation followed by the population size and the age of the oldest individual, post-mortality):

```
1: 10 (0)
2: 60 (1)
3: 360 (2)
4: 513 (3)
5: 473 (4)
6: 460 (4)
7: 480 (3)
8: 504 (3)
9: 505 (4)
```

The population size is around `500`, the oldest individual usually `3` or `4`. So far so good. Now let's look at the output at the end of the run, in a run in which the beneficial mutation fixes:

```
1996: 768 (4)
1997: 771 (3)
1998: 781 (4)
1999: 763 (3)
2000: 802 (4)
```

The population size is now fluctuating around `760` to `800`, although the typical age of the oldest individual is still `3` to `4`. What happened to our carrying capacity of `500`?

The answer lies in the fitness values calculated by SLiM. Two things affect fitness in this model. One is density-dependent mortality, as embodied in the `fitnessScaling` value set by the `early()` callback. When the population is above carrying capacity (as it is in every generation from `4` onwards, in this model, due to the many juveniles), this scaling value will be less than `1.0`; given how many juveniles this model makes, it is probably usually `0.2` or lower, in fact. The other thing affecting fitness is the beneficial mutation; since it is dominant, it gives any individual possessing it a fitness effect of `1.5` since its selection coefficient is `0.5`. These fitness effects are multiplicative, so once the beneficial mutation has fixed, every individual will have a fitness value of approximately `0.2 * 1.5`, or `0.3`. This means, in effect, that fewer individuals will die, and the carrying capacity will increase. Which is precisely what we see.

This may be unexpected for those who are used to the world of Wright-Fisher models, but it makes good biological sense. If every individual possesses a mutation that makes them more fit – more likely to survive – then the population size *ought* to increase. If there is some reason why that shouldn't happen, such as a hard limit on the amount of available food, then you ought to add that biological detail to your model explicitly. This sort of thing is precisely why the individual-based nature of nonWF models, with emergent dynamics for things like population size and age structure, has the potential to be more biologically realistic.

This point becomes even more pointed if you write a model in which new beneficial mutations can arise spontaneously. In such a nonWF model, absolute fitness would increase a little bit more with every new beneficial mutation, and the population would evolve toward a "Darwinian demon" with infinite absolute fitness and infinite population size. Fundamentally, that is just a more extreme case of the same situation as in this recipe: if your model tells SLiM that absolute fitness has increased, population size will increase concomitantly. If you want some mechanism to hold that tendency in check, you need to add that mechanism to your model yourself.

In this recipe, for example, it would certainly be possible to force the model to maintain the same carrying capacity throughout, but trying to do so might just expose how biologically unrealistic that constraint really is. If the carrying capacity is the same before and after the beneficial mutation fixes, that means that the survival probability is the same (assuming we don't alter reproductive output). So once the beneficial mutation has fixed, it apparently no longer confers any benefit to the carrier – even though it *did* confer a benefit (relative to the non-carrier individuals) earlier on, before the beneficial mutation had fixed. What has changed? Nothing about the environment, and the population size has not changed (since we are making the carrying capacity fixed) – and yet somehow, almost magically, the fitness benefit that used to exist has evaporated. The only thing that has changed, in fact, is that now *other* individuals also possess the mutation, whereas early on in the sweep few or none did. And that suggests one way that we could make the carrying capacity fixed in this model: add in negative frequency-dependent selection (see section 9.4.1). Maybe there's a good biological reason for that: limited resources, for example, such that a mutation that makes an individual better at obtaining those resources confers less and less benefit as the mutation gets more and more common. If that's the biology, then great, model that. But if one is tempted to hold the population size fixed simply because one is used to Wright-Fisher models that hold the population size fixed – not for any biological reason – then it would probably be best to think twice. The lesson of this recipe, in other words, might be: Model the biology, not your own modeling assumptions. Let emergent dynamics emerge.

Or if you really want to stay in the world of Wright-Fisher assumptions, then write a WF model; there's nothing wrong with that, as long as you understand the assumptions you're making.

15.5 A metapopulation extinction-colonization model

Our models so far have been of a single subpopulation, but nonWF models have many advantages for modeling migration that we will explore in this recipe and the next. Here, we will model a metapopulation undergoing local extinctions and then re-colonizations from other subpopulations. This would be difficult to implement in a WF model, because population size is not allowed to go to zero (that signifies removal of the subpopulation from the model), and because re-colonization by migrants does not happen naturally (it would have to be done as re-creation of the extinct subpopulation using `addSubpopSplit()`, and the founders could come only from a single source subpopulation). In a nonWF model, however, this is quite straightforward. For simplicity, we will model a non-spatial metapopulation in which every subpopulation is connected to every other by migration of equal strength:

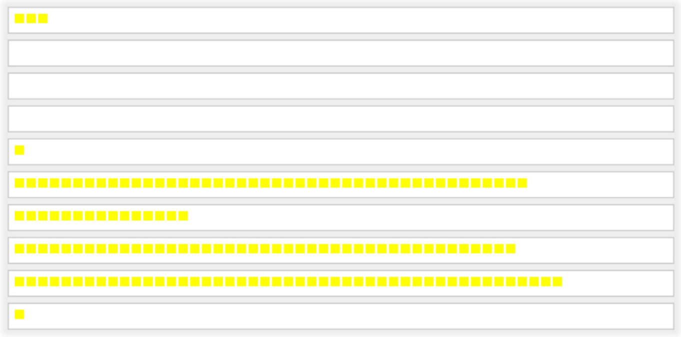
```
initialize() {
    initializeSLiMModelType("nonWF");
    defineConstant("K", 50);     // carrying capacity per subpop
    defineConstant("N", 10);     // number of subpopulations
    defineConstant("m", 0.01);   // migration rate
    defineConstant("e", 0.1);    // subpopulation extinction rate

    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;

    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);
}
reproduction() {
    subpop.addCrossed(individual, subpop.sampleIndividuals(1));
}
1 early() {
    for (i in 1:N)
      sim.addSubpop(i, (i == 1) ? 10 else 0);
}
early() {
    // random migration
    nIndividuals = sum(sim.subpopulations.individualCount);
    nMigrants = rpois(1, nIndividuals * m);
    migrants = sample(sim.subpopulations.individuals, nMigrants);

    for (migrant in migrants)
    {
      do dest = sample(sim.subpopulations, 1);
      while (dest == migrant.subpopulation);

      dest.takeMigrants(migrant);
    }

    // density-dependence and random extinctions
    for (subpop in sim.subpopulations)
    {
      if (runif(1) < e)
        subpop.fitnessScaling = 0.0;
      else
        subpop.fitnessScaling = K / subpop.individualCount;
    }
}
late() {
    if (sum(sim.subpopulations.individualCount) == 0)
      stop("Global extinction in generation " + sim.generation + ".");
}
2000 late() {
    sim.outputFixedMutations();
}
```

We start off by defining constants for the carrying capacity `K`, the subpopulation count `N`, the per-individual migration rate `m`, and the per-generation probability `e` of a local extinction event in a given subpopulation, such as might occur due to a forest fire or flood. We then set up a neutral nonWF model with simple offspring generation (one offspring per individual per generation), and create `N` subpopulations. The first subpopulation begins with `10` individuals; the rest begin empty, awaiting migrants (which is legal in nonWF models; subpopulations can be empty). At the end of the model, we have a `late()` event that halts the model with a message if all subpopulations have gone extinct; if we make it to generation `2000` we output fixed mutations and stop.

The interesting code is in the middle, in the large `early()` event. This first implements random migration by drawing the number of migrants from a Poisson distribution and then sampling migrants at random from the full population; this gives each individual the same probability `m` of migrating, and is more efficient than doing a random draw for each individual. It then loops through the chosen migrants, finds their destination subpopulation (ensuring that it is not the subpopulation the migrant already occupies), and finally calls `takeMigrants()` to move the individual to its new home. The `takeMigrants()` call removes the individual from its old subpopulation and adds it immediately to the target subpopulation; it is the way that migration is implemented in nonWF models. Note that the design of this code avoids choosing and moving a migrant, and then accidentally choosing that same individual as a migrant again and moving it again; all migrants are selected, and then all migrants are moved. This design is generally a good idea, to avoid accidentally skewing the migration rates for subpopulations away from their intended rates. The `migrant` property of `Individual` could also be used to prevent this, together with the ability of `sampleIndividuals()` to select individuals that have not already migrated.

The second half of the `early()` event implements both density-dependence and random local extinction events. It draws from a random uniform distribution, and if the draw is less than the probability of local extinction `e`, it sets the subpopulation's `fitnessScaling` property to zero, effectively reducing the fitness of all individuals in the subpopulation to zero and thus killing them all. The rest of the time, `fitnessScaling` is set based on subpopulation density as usual, producing growth up to the carrying capacity `K` for each subpopulation.

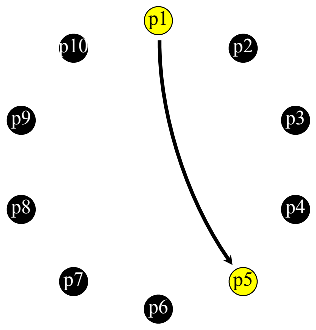
When run, this model produces fairly realistic extinction-colonization dynamics; after a subpopulation is hit by an extinction event, it will eventually be recolonized and then undergo rapid growth until reaching carrying capacity again. Here's a snapshot from SLiMgui mid-run:



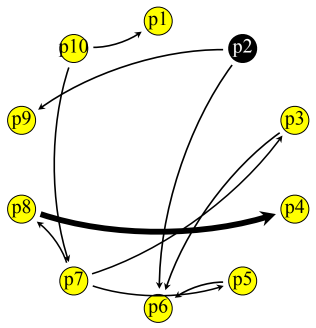
Three subpopulations are presently empty, two have just been recolonized by a single migrant, two others are at intermediate stages of growth, and three are roughly at carrying capacity (which is, as usual in nonWF models, not a hard limit). Note that all individuals are displayed here in yellow, because SLiMgui normalizes away subpopulation-level `fitnessScaling` constants in order to display individual fitness prior to density-dependent scaling, since that is generally what one is interested in seeing; it does the same thing, in a sense, in WF models too. In fact, though, the populations below carrying capacity have a fitness greater than `1.0` that is driving their growth, and the populations at carrying capacity have a fitness less than `1.0` that compensates for their births to keep them at equilibrium.

If the migration rate is too low, or the extinction rate is too high, the whole population will often go extinct; but with less apocalyptic parameter values recolonization will keep up with extinction and the population will persist (for a while, anyway; the design of the extinction events in this model means that sudden global extinction of all subpopulations will happen with probability `e^N`, so eventually the model will always go extinct as long as `e > 0`).

A nice feature in SLiMgui that is worth pointing out is that it keeps metrics regarding the behavior of your model, and can display those metrics for you. You might recall the Population Visualization graph that SLiMgui can display to show population sizes, fitnesses, and migration patterns (see, e.g., sections 5.1.3 and 5.2.1). In nonWF models the migration rates between subpopulations are not set ahead of time, but are instead an emergent property of the model, as we have seen in this recipe. SLiMgui will monitor the actual migration generated in the running nonWF model and display it in the Population Visualization graph. For example, here's the pattern of migration in generation 3 of a run of this recipe:



This shows that `p5` has just received a migrant from `p1`; this is the initial colonization of `p5`, in fact. The other subpopulations are black because they are empty at this point. Later in the run, it might look like this instead:



Lots is going on here; `p8` sent a relatively large proportion of its population to `p4`, by chance (thus the thicker arrow) – maybe two or three or four migrants. Migrants were sent from `p2` to both `p6` and `p9`, and then, immediately after, `p2` got hit by an extinction event. And so forth. This facility can be quite useful for debugging migration code, or for seeing how the pattern of migration changes over time when it depends upon other model state (as in the next recipe).

In fact, SLiMgui monitors and displays other emergent metrics in nonWF models, too. In the subpopulation table, for example, where things like the cloning rate, selfing rate, and sex ratio are displayed for WF models, the actual, observed metrics for those properties will be displayed by SLiMgui for nonWF models. This particular recipe is not a good showcase for that feature, however, since it is an asexual model involving only biparental mating.

15.6 Habitat choice

In the previous section migration in nonWF models using the `takeMigrants()` method was introduced. Here we will further explore migration in nonWF models. In WF models, as you may recall, migration occurs during offspring generation: parents from one subpopulation mate, but their offspring gets added to a different subpopulation if it migrates. This type of juvenile migration is the only possibility in WF models; but nonWF models are not restricted in that way, and here we will construct a nonWF model of migration that can occur at any age. Each generation, individuals will choose which environment they will live in, a phenomenon commonly called "habitat choice". All else equal, they will prefer the environment they are already in; but if the other environment is better for them, then with a non-zero probability they will decide to move. This model will also include variation in the individual propensity to migrate, and emergent variation in the total number of migrants in each generation – both difficult to capture in WF models.

The basic design of this model is patterned after recipe in section 9.2: we have two subpopulations, `p1` and `p2`, and a mutation type, `m2`, that represents relatively rare mutations that are beneficial in `p1` but deleterious in `p2`. For balance, let's also have a mutation type `m3` for mutations that are deleterious in `p1` but beneficial in `p2`. Finally, let's throw a spanner into the works by making offspring initially go to a random subpopulation, not always to the subpopulation of their parents (perhaps representing some sort of shared spawning environment from which juveniles initially disperse randomly).

Here is the model except for the habitat choice code:

```
initialize() {
    initializeSLiMModelType("nonWF");
    defineConstant("K", 500);

    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;
    initializeMutationType("m2", 0.5, "e", 0.1);   // deleterious in p2
    m2.color = "red";
    initializeMutationType("m3", 0.5, "e", 0.1);   // deleterious in p1
    m3.color = "green";

    initializeGenomicElementType("g1", c(m1,m2,m3), c(0.98,0.01,0.01));
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);
}
reproduction() {
    dest = sample(sim.subpopulations, 1);
    dest.addCrossed(individual, subpop.sampleIndividuals(1));
}
1 early() {
    sim.addSubpop("p1", 10);
    sim.addSubpop("p2", 10);
}
early() {
    p1.fitnessScaling = K / p1.individualCount;
    p2.fitnessScaling = K / p2.individualCount;
}
fitness(m2, p2) { return 1/relFitness; }
fitness(m3, p1) { return 1/relFitness; }
```

```
1000 late() {
    for (id in 1:2)
    {
       subpop = sim.subpopulations[sim.subpopulations.id == id];
       s = subpop.individualCount;
       inds = subpop.individuals;
       c2 = sum(inds.countOfMutationsOfType(m2));
       c3 = sum(inds.countOfMutationsOfType(m3));
       catn("subpop " + id + " (" + s + "): " + c2 + " m2, " + c3 + " m3");
    }
}
```

The structure of this model is quite predictable. The `initialize()` callback sets up the local-adaptation `m2` and `m3` mutation types, and the two `fitness()` callbacks render mutations of those types deleterious in one or the other subpopulation. The `reproduction()` callback generates each new offspring in a randomly chosen subpopulation, representing random juvenile dispersal from a spawning environment as mentioned above. We also have the usual nonWF density-dependent fitness scaling, and we have an output event that prints information about the two subpopulations (as we will discuss below).

The interesting part, then, is the large `early()` event for habitat choice, which should be inserted just above the density-dependence `early()` event (so that density-dependence is based upon post-migration subpopulation sizes, not the pre-migration sizes):

```
early() {
    // habitat choice
    inds = sim.subpopulations.individuals;
    inds_m2 = inds.countOfMutationsOfType(m2);
    inds_m3 = inds.countOfMutationsOfType(m3);
    pref_p1 = 0.5 + (inds_m2 - inds_m3) * 0.1;
    pref_p1 = pmax(pmin(pref_p1, 1.0), 0.0);
    inertia = ifelse(inds.subpopulation.id == 1, 1.0, 0.0);
    pref_p1 = pref_p1 * 0.75 + inertia * 0.25;
    choice = ifelse(runif(inds.size()) < pref_p1, 1, 2);
    moving = inds[choice != inds.subpopulation.id];
    from_p1 = moving[moving.subpopulation == p1];
    from_p2 = moving[moving.subpopulation == p2];
    p2.takeMigrants(from_p1);
    p1.takeMigrants(from_p2);
}
```

The logic of this event goes through several steps, but is not complicated. First it gets a vector of all individuals, and derives vectors of the number of `m2` and `m3` mutations possessed by each individual; each of these is a vector of counts corresponding to the original vector of individuals. It then computes a vector of habitat preferences for each individual: starting from a neutral preference of `0.5`, the more `m2` mutations an individual has, and the fewer `m3` mutations it has, the more that individual prefers `p1` over `p2`. Each `m2` or `m3` mutation shifts its preference by only 10%, however, so these preferences are not initially very strong; and this preference is clamped to the range [`0.0`, `1.0`] so that even once many m2 and m3 mutations exist this preference is still bounded. Next the script computes an "inertial" habitat preference for `p1` over `p2`, expressing a simple desire not to move; for individuals presently in `p1` this is `1.0`, whereas for those in `p2` it is `0.0`. The final habitat preference is computed as a weighted average of these two considerations; in this recipe the genetically-based preference is given a weight of `0.75` and the inertial preference is given a weight of `0.25`, making individuals fairly strongly inclined to move, but this balance is a free parameter in the model. Next, we actually decide which subpopulation each individual chooses, by comparing a random uniform draw to the individual's weighted preference. (Note that these calculations continue to be vectorized; this event handles all migration with a single sequence of calculations.) The `moving` vector is the subset of individuals that chose a different subpopulation than they currently occupy; these individuals will migrate, while the rest stay put. The script then finds which migrants are currently in `p1` (moving to `p2`) and which are in `p2` (moving to `p1`), and then, finally, it makes `takeMigrants()` calls that actually move those individuals. This method simply removes the given individuals from their current subpopulation and inserts them into the target subpopulation. One could implement habitat choice in many different ways, embodying different decision-making processes for the individuals involved, different degrees of knowledge about the available habitat options, different approaches to the stochasticity of the choice, and so forth; this is just one simple algorithm for demonstration purposes.

Without any migration (if the habitat-choice `early()` event is commented out, in other words), this model will "flip" to favor one subpopulation based upon the `m2` and `m3` mutations that happen to do well early on; the successful subpopulation will grow very large (as its carrying capacity increases, because so many individuals carry mutations that are beneficial in that environment; see section 15.4), whereas the unsuccessful subpopulation will shrink toward zero (swamped by vast numbers of offspring from the other subpopulation that are massively maladapted and immediately die). Output from that version of the model typically looks like this:

```
subpop 1 (191): 0 m2, 1180 m3
subpop 2 (1314): 0 m2, 8072 m3
```

The model has "flipped" toward subpop `p2`, which is now `1314` individuals to `p1`'s 191 individuals. There are quite a large number of copies of `m3`-type alleles in play, whereas there are no `m2`-type alleles. Subpop `p1` will never be able to dig itself out of this hole, since it gets swamped with new offspring from `p2` every generation that carry `m3` alleles and not `m2` alleles, and any `m2` alleles it manages to scrape together get diluted into `p2` and selected out. If the model runs longer, `p1` will effectively go extinct except for whatever cohort of confused migrants arrives to repopulate it in each generation.

But with the `early()` event that implements habitat choice, the story is very different. Now, if the probability of correct habitat choice is sufficiently high, the subpopulations can diverge; even though they still sabotage each other with maladapted offspring, those offspring tend to migrate over to the subpopulation where they are more fit. One subpop often grows significantly larger than the other, but the model no longer "flips"; the smaller subpop is much more able to persist. Output from the model with habitat choice:

```
subpop 1 (620): 2838 m2, 173 m3
subpop 2 (1065): 149 m2, 7177 m3
```

The subpopulations are now much closer in size, and show clear divergence in their `m2` and `m3` profiles. In SLiMgui the different haplotypes of the two subpopulations are immediately visible, since the `m2` and `m3` mutations have been given different colors. Subpopulation `p2` is larger here, since there are more `m3` alleles segregating, but it is no longer swamping `p1` or diluting away the `m2` alleles to such an extent that `p1` can't also thrive, and if new `m2` mutations arise they will often be able to establish themselves in `p1` so the current imbalance may not even persist. Divergence here is much more successful, and in fact it is effective enough that neutral sites will diverge as well, indicating that this mechanism is sufficient to generate substantial reproductive isolation. The degree of isolation will depend upon parameters such as the strength of habitat choice versus the "inertial" preference for the current habitat, and the strength of the divergent selection on the `m2` and `m3` alleles, of course.

This recipe goes beyond the capabilities of WF models in several important ways. One way is that individuals of all ages migrate in this model, not just newly created juveniles as in WF models. Indeed, in this model the same individual may just back and forth between `p1` and `p2` several times, if it has no strong preference. A second way is that the migratory behavior here is based upon individual genetic state. This is possible to implement in WF models, using a `modifyChild()` callback that accepts or rejects proposed migrant offspring based upon their genetics, but in practice it would be difficult and problematic. A third way is that the amount of migration in this model is itself condition-dependent; if there are many maladapted individuals, there will be many migrants, if fewer, fewer migrants. This would be difficult to do in a WF model since SLiM then fulfills a pre-set migration rate; that pre-set rate would have to be carefully predicted and altered in every generation in order to try to foretell the desired result from offspring generation, which would be very clumsy if it worked at all. Migration is an individual choice, so it is much simpler and more natural to model it as such, as nonWF models do.

Many interesting extensions to this model could be made. For example, one could impose a fitness cost upon migration, and then allow the propensity for migration to itself evolve by making the weighting between habitat choice and "inertia" depend upon a quantitative trait. Individuals that chose to migrate too often would suffer a high cost, but those that did not migrate at all, even when strongly maladapted, would also be penalized, and so some intermediate, optimal migration tendency would perhaps tend to evolve. Such a model would rely heavily upon the advantages of the individual-based migration of nonWF models; it would be very difficult to fit it into the WF paradigm.

15.7 Evolutionary rescue after environmental change

The evolutionary response of a population to environmental change, and the probability of extinction if that response is insufficient, is the subject of an important class of models called "evolutionary rescue" models – particularly relevant in this era of anthropogenic climate change. Evolutionary rescue can be based upon standing genetic variation, new mutations that provide new adaptive potential, or genetic variation brought in by migrants. Here we will look at a QTL-based model of evolutionary rescue that may (or may not) occur as a result of both standing genetic variation and new mutations. This model is based heavily upon other QTL models in this manual (see sections 13.1, 13.10, and 13.17), adapted here to illustrate that QTL-based approaches are entirely compatible with nonWF models.

Let's look at this model piece by piece, beginning with `initialize()`:

```
initialize() {
    initializeSLiMModelType("nonWF");
    defineConstant("K", 500);
    defineConstant("opt1", 0.0);
    defineConstant("opt2", 10.0);
    defineConstant("Tdelta", 10000);

    initializeMutationType("m1", 0.5, "n", 0.0, 1.0);  // QTL
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);
}
```

For simplicity and speed, we define only a QTL mutation type, `m1`; this model has no neutral mutations in it (but of course they would be trivial to add). Each QTL is drawn from a normal distribution centered on `0.0` with a standard deviation of `1.0` (which are important parameters for this model, since the exact nature of the standing genetic variation and mutational variance will be important). Besides this, the initialization is quite standard. We set up defined constants for the carrying capacity (`K`), for the phenotypic optimum before and after environmental change (`opt1` and `opt2`), and for the time when the environmental change will occur (`Tdelta`).

Next we set up our reproduction and our initial population:

```
reproduction() {
    subpop.addCrossed(individual, subpop.sampleIndividuals(1));
}
1 early() {
    sim.addSubpop("p1", 500);
}
```

This is boilerplate, except that here we start at the carrying capacity so that if we configure the environmental change to occur immediately at the beginning of the model (as we will try below), the population is not at a disadvantage due to not yet having grown to capacity.

We need our QTL machinery, which is quite simple in this model:

```
early() {
    // QTL-based fitness
    inds = sim.subpopulations.individuals;
    phenotypes = inds.sumOfMutationsOfType(m1);
    optimum = (sim.generation < Tdelta) ? opt1 else opt2;
    deviations = optimum - phenotypes;
    fitnessFunctionMax = dnorm(0.0, 0.0, 5.0);
    adaptation = dnorm(deviations, 0.0, 5.0) / fitnessFunctionMax;
    inds.fitnessScaling = 0.1 + adaptation * 0.9;
    inds.tagF = phenotypes;   // just for output below

    // density-dependence with a maximum benefit at low density
    p1.fitnessScaling = min(K / p1.individualCount, 1.5);
}
fitness(m1) { return 1.0; }
```

The `fitness(m1)` callback makes the direct fitness effect of `m1` mutations neutral, as usual in such QTL models; the only effect of QTL mutations on fitness is indirect, through their effect on individual phenotypic values.

The `early()` event calculates individual phenotypes as the sum of the effects of all QTLs possessed by the individual. It then decides which phenotypic optimum is in effect, calculates the deviation of each individual from that optimum, and calculates the degree of adaptation of each individual from that using `dnorm()` (normalizing the adaptation values to the range (`0`,`1`] with `fitnessFunctionMax`). Finally, `fitnessScaling` values for individuals are set based upon their adaptation; a perfectly adapted individual will have an adaptation value of `1.0` and thus a `fitnessScaling` value of `1.0`, whereas an infinitely maladapted individual will have an adaptation value of `0.0` and thus a `fitnessScaling` value of `0.1`, the "floor" in this model (a crucial parameter that will influence the probability of evolutionary rescue).

The `early()` event also, at the end, implements density-dependent population regulation. This is done in the usual way, except that a maximum of `1.5` is imposed with `min()`. In principle, this sort of correction ought to have been imposed on all our other nonWF models, but in models that do not include deleterious mutations, and which are not expected to spend time at low density, it is unimportant. The rationale for the correction is that being at low population density does convey *some* benefit (assuming the absence of Allee effects, as we have been doing), allowing individuals to survive and reproduce at their full capacity even when they carry some minor deleterious mutations that would negatively impact them if they were in a population at full carrying capacity – but this benefit is surely limited! Typically, a population will not thrive if it carries many large-effect deleterious mutations, even if it is released from all density-dependent pressures. The maximum of `1.5` here embodies that intuitive fact, by stating that the fitness benefit of low density can never be more than a multiplicative fitness effect of `1.5`. (This is another important model parameter, of course.)

Finally, we have our output and termination events:

```
late() {
    if (p1.individualCount == 0)
    {
       // stop at extinction
       catn("Extinction in generation " + sim.generation + ".");
       sim.simulationFinished();
    }
    else
    {
       // output the phenotypic mean and pop size
       phenotypes = p1.individuals.tagF;
       
       cat(sim.generation + ": " + p1.individualCount + " individuals");
       cat(", phenotype mean " + mean(phenotypes));
       if (size(phenotypes) > 1)
          cat(" (sd " + sd(phenotypes) + ")");
       catn();
    }
}
20000 late() { sim.simulationFinished(); }
```

The simulation checks for extinction in every generation, and stops with a termination message. Otherwise, it prints a summary with the current population size, and the mean and standard deviation of the distribution of phenotypes. If extinction is avoided, the model stops after generation `20000`.

Running this recipe as configured, we begin with no genetic diversity at all:

```
1: 500 individuals, phenotype mean 0 (sd 0)
2: 529 individuals, phenotype mean 0.000628046 (sd 0.107673)
3: 499 individuals, phenotype mean -0.00650893 (sd 0.152125)
4: 470 individuals, phenotype mean -0.00802766 (sd 0.188649)
5: 497 individuals, phenotype mean 0.00997383 (sd 0.225336)
...
```

By generation `10000`, when the environment changes, we have built up some standing genetic variation – although really not much more than we had just a few generations in:

```
...
9995: 493 individuals, phenotype mean -0.101779 (sd 0.616717)
9996: 498 individuals, phenotype mean -0.139806 (sd 0.592579)
9997: 518 individuals, phenotype mean -0.146021 (sd 0.55228)
9998: 493 individuals, phenotype mean -0.127487 (sd 0.537018)
9999: 500 individuals, phenotype mean -0.139612 (sd 0.531529)
```

Then we hit generation `10000`, the optimum suddenly changes to `10.0`, and things get very ugly very fast:

```
10000: 123 individuals, phenotype mean -0.095242 (sd 0.560048)
10001: 77 individuals, phenotype mean 0.0100077 (sd 0.628869)
10002: 54 individuals, phenotype mean -0.191957 (sd 0.624277)
10003: 35 individuals, phenotype mean -0.0215701 (sd 0.55838)
10004: 18 individuals, phenotype mean 0.211882 (sd 0.862124)
10005: 7 individuals, phenotype mean 0.196655 (sd 1.07714)
10006: 5 individuals, phenotype mean 0.200521 (sd 0.144637)
10007: 3 individuals, phenotype mean 0.123028 (sd 0.0531924)
10008: 2 individuals, phenotype mean 0.153739 (sd 0)
10009: 1 individuals, phenotype mean 0.153739
Extinction in generation 10010.
```

The population evolved toward the new optimum, but not quickly enough to overcome its crash in population size, and it went extinct in only eleven generations. However, this is actually not the typical outcome for the model. Here's another run just before the environmental change:

```
...
9995: 494 individuals, phenotype mean 0.152236 (sd 0.576086)
9996: 511 individuals, phenotype mean 0.144287 (sd 0.590623)
9997: 503 individuals, phenotype mean 0.151616 (sd 0.616162)
9998: 489 individuals, phenotype mean 0.115655 (sd 0.617752)
9999: 508 individuals, phenotype mean 0.11127 (sd 0.611983)
```

And here's what happened after:

```
10000: 112 individuals, phenotype mean 0.373886 (sd 0.714775)
10001: 84 individuals, phenotype mean 0.394201 (sd 0.768464)
10002: 58 individuals, phenotype mean 0.447692 (sd 0.855927)
10003: 48 individuals, phenotype mean 0.689259 (sd 0.925998)
10004: 31 individuals, phenotype mean 0.877411 (sd 1.12496)
10005: 29 individuals, phenotype mean 1.12907 (sd 1.10892)
10006: 25 individuals, phenotype mean 1.50111 (sd 1.29306)
10007: 20 individuals, phenotype mean 1.45553 (sd 1.30944)
10008: 17 individuals, phenotype mean 1.88997 (sd 1.42636)
10009: 15 individuals, phenotype mean 2.67739 (sd 1.60781)
10010: 16 individuals, phenotype mean 2.92828 (sd 1.58097)
10011: 26 individuals, phenotype mean 3.32725 (sd 1.53169)
10012: 35 individuals, phenotype mean 3.87526 (sd 1.24333)
10013: 56 individuals, phenotype mean 4.13832 (sd 1.10771)
10014: 98 individuals, phenotype mean 4.27727 (sd 1.12148)
10015: 158 individuals, phenotype mean 4.54129 (sd 0.940975)
10016: 285 individuals, phenotype mean 4.66029 (sd 0.881386)
10017: 321 individuals, phenotype mean 4.84315 (sd 0.807692)
10018: 314 individuals, phenotype mean 4.98733 (sd 0.726859)
10019: 355 individuals, phenotype mean 5.08917 (sd 0.712417)
10020: 337 individuals, phenotype mean 5.18797 (sd 0.735515)
10021: 328 individuals, phenotype mean 5.28416 (sd 0.70728)
...
```

The population size dips down as low as `15` individuals, and the phenotypic optimum still seems quite distant, but it manages to stage a full recovery; it's back up to carrying capacity within about a hundred generations.

In twenty runs of the model, extinction occurred nine times and evolutionary rescue occurred eleven times. We can test the importance of standing genetic variation for rescue by simply setting `Tdelta` to `0`, making the optimum be `10.0` from the start of the model with no chance for standing genetic variation to build up; in this variant of the model, extinction occurred sixteen out of twenty times, rescue only four times. So: probably important. Which might seem a bit surprising, since the variance in phenotype is really not large in generation 9999; but there are, nevertheless, a lot of useful QTLs that can be brought together by recombination and applied to the problem of rapid evolution.

We can also test the importance of new mutations to evolutionary rescue, by setting the mutation rate to 0.0 when the environment changes; the population will then have nothing but standing variation at its disposal. A proper test of this would require many runs of the model, but I can state that evolutionary rescue does sometimes occur from the standing variation alone. Here's the population just before the change, in one run of that variant of the model:

```
...
9995: 462 individuals, phenotype mean -0.020969 (sd 0.842111)
9996: 489 individuals, phenotype mean -0.0413428 (sd 0.843401)
9997: 488 individuals, phenotype mean 0.0205512 (sd 0.805816)
9998: 496 individuals, phenotype mean -0.0103366 (sd 0.744229)
9999: 488 individuals, phenotype mean -0.0287371 (sd 0.829185)
```

And here's the recovery, in all its glory:

```
10000: 110 individuals, phenotype mean 0.0798129 (sd 0.941083)
10001: 86 individuals, phenotype mean 0.199899 (sd 0.936995)
10002: 70 individuals, phenotype mean 0.369471 (sd 0.986702)
10003: 52 individuals, phenotype mean 0.643418 (sd 1.1836)
10004: 46 individuals, phenotype mean 0.780035 (sd 1.25709)
10005: 42 individuals, phenotype mean 1.23978 (sd 1.55453)
10006: 43 individuals, phenotype mean 1.86605 (sd 1.7264)
10007: 39 individuals, phenotype mean 2.62644 (sd 1.805)
10008: 48 individuals, phenotype mean 3.24882 (sd 1.82018)
10009: 67 individuals, phenotype mean 3.83253 (sd 1.69954)
10010: 101 individuals, phenotype mean 4.43066 (sd 1.53875)
10011: 165 individuals, phenotype mean 4.76209 (sd 1.42616)
10012: 289 individuals, phenotype mean 5.14574 (sd 1.27371)
10013: 325 individuals, phenotype mean 5.48173 (sd 1.19875)
10014: 360 individuals, phenotype mean 5.79835 (sd 1.02552)
10015: 369 individuals, phenotype mean 5.93227 (sd 0.973104)
10016: 386 individuals, phenotype mean 5.96707 (sd 0.959739)
10017: 372 individuals, phenotype mean 6.00515 (sd 0.953603)
10018: 371 individuals, phenotype mean 6.2132 (sd 0.813674)
10019: 364 individuals, phenotype mean 6.31304 (sd 0.698918)
10020: 380 individuals, phenotype mean 6.37598 (sd 0.604686)
10021: 427 individuals, phenotype mean 6.45539 (sd 0.471641)
10022: 370 individuals, phenotype mean 6.51224 (sd 0.363968)
10023: 412 individuals, phenotype mean 6.53184 (sd 0.305041)
10024: 415 individuals, phenotype mean 6.54332 (sd 0.277311)
10025: 404 individuals, phenotype mean 6.53433 (sd 0.299239)
10026: 380 individuals, phenotype mean 6.55845 (sd 0.234658)
10027: 386 individuals, phenotype mean 6.55116 (sd 0.256157)
10028: 421 individuals, phenotype mean 6.53684 (sd 0.293376)
10029: 390 individuals, phenotype mean 6.53791 (sd 0.29318)
10030: 401 individuals, phenotype mean 6.53193 (sd 0.307162)
10031: 403 individuals, phenotype mean 6.55492 (sd 0.248401)
10032: 418 individuals, phenotype mean 6.57826 (sd 0.165723)
10033: 428 individuals, phenotype mean 6.57869 (sd 0.163795)
10034: 399 individuals, phenotype mean 6.58121 (sd 0.151873)
10035: 420 individuals, phenotype mean 6.5856 (sd 0.128374)
10036: 402 individuals, phenotype mean 6.58132 (sd 0.15131)
10037: 422 individuals, phenotype mean 6.58565 (sd 0.128071)
10038: 419 individuals, phenotype mean 6.59647 (sd 0)
```

This is somewhat remarkable, since the new optimum is more than twelve standard deviations away from the population's phenotypic mean at the moment of the environmental change. The population fixes for a single QTL haplotype by the end (thus, a standard deviation of `0`), and that haplotype provides a phenotype of 6.59647, which is almost exactly eight standard deviations away from where it started – quite impressive. So rescue appears to be possible from standing variation alone (sometimes), and from new mutations alone (sometimes), and most often from both together (but still, only sometimes).

These outcomes will depend – perhaps quite sensitively – on the various parameters of the model, such as the carrying capacity, the distance from the old optimum to the new one, the mutational distribution and rate, the "floor" of the fitness function, and the maximum fitness benefit from low population density. There are other implicit parameters here too, such as the level of individual fecundity and the variance in that fecundity (here, zero). This is also a hermaphroditic model, and hermaphroditic selfing is not prevented; switching to a sexual model would make evolutionary rescue that much more difficult, since a non-zero number of both males and females would need to be present in every generation. In short, gaining a proper understanding of the dynamics of even this rather simple model would require some real work.

Nevertheless, the population dynamics of the model seem fairly realistic, and adding in even more realism – sex, Allee effects, gradual environmental change instead of a sudden shift, etc. – would not be difficult. Simulating this in a WF model would be more difficult to do with this level of realism, since the population size would have to be set explicitly in every generation (rather than being emergent from the birth/death dynamics), and would be fulfilled deterministically by SLiM rather than exhibiting the natural stochastic variation around the carrying capacity that this nonWF model exhibits.

Another interesting direction to take this model would be to use it to investigate the advantages of sexual versus clonal reproduction. It has long been theorized that one of the disadvantages of clonal reproduction is the difficulty of responding to environmental changes without the ability to recombine parental genomes to bring adaptive alleles together onto the same chromosome. One could experiment, in this model, with the effect of sexual versus clonal reproduction on evolutionary rescue – and even the evolution of the reproductive mode in response to environmental change. One could add a second QTL-based trait (see section 13.17) that governed the probability that an individual would clone or reproduce sexually, and see whether environmental change – perhaps cyclical or unpredictable – would provide enough of an advantage to sexual reproduction to prevent clonal reproduction from taking over the population. This would be straightforward to simulate in a nonWF model, since each individual generates its own offspring and can choose its own reproductive mode, based upon genetics or anything else. It would be considerably harder to implement in a WF model since the reproductive mode is controlled only by the subpopulation-wide cloning rate and cannot easily be influenced by individual genetics or other state.

15.8 Pollen flow

Plants reproduce sexually when a pollen grain from a flower reaches another (or perhaps the same) flower and fertilizes an ovule. The pollen might be transmitted by a pollinator, or by wind or water or other vectors. An important aspect of plant reproductive biology, then, is that pollen from a flower in one subpopulation might end up fertilizing a flower in a different subpopulation. In animals, gene flow between subpopulations generally results from the migration of individuals, such as we modeled in sections 15.5 and 15.6 (and in many WF recipes as well). In plants, in contrast, gene flow between subpopulations usually results from the migration of gametes (or, in some species, gametophytes).

Pollen flow between subpopulations is a very important aspect of plant reproduction, then, but it is quite difficult to model with a WF model in SLiM since offspring in WF models always come from the mating of two individuals in the same subpopulation. Another advantage of nonWF models, then, is that they can easily simulate pollen flow, because sexual reproduction can involve any two individuals in the model.

This will be a very quick model since the concept is very simple and we have no complicated analysis to do with the results:

```
initialize() {
    initializeSLiMModelType("nonWF");
    defineConstant("K", 200);

    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;

    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);
}
reproduction() {
    // determine how many ovules were fertilized, out of the total
    fertilizedOvules = rbinom(1, 30, 0.5);

    // determine the pollen source for each fertilized ovule
    other = (subpop == p1) ? p2 else p1;
    pollenSources = ifelse(runif(fertilizedOvules) < 0.99, subpop, other);

    // generate seeds from each fertilized ovule
    // the ovule belongs to individual, the pollen comes from source
    for (source in pollenSources)
      subpop.addCrossed(individual, source.sampleIndividuals(1));
}
1 early() {
    sim.addSubpop("p1", 10);
    sim.addSubpop("p2", 10);
}
early() {
    for (subpop in sim.subpopulations)
      subpop.fitnessScaling = K / subpop.individualCount;
}
10000 late() {
    sim.outputFixedMutations();
}
```

Most of this model is boilerplate that should be familiar by now. The interesting part is the `reproduction()` callback. Here we model hermaphroditic (or perhaps monoecious) flowering plants, so we do not model separate sexes, but we assume that selfing is no more common than would be expected by chance (when an individual happens to choose itself as a pollen source in this `reproduction()` code, which we do not prevent here). Each flower has `30` ovules, each with a probability of `0.5` of being fertilized, so the total number of fertilized ovules is drawn from a binomial distribution. We then determine the subpopulation that supplied the pollen for each of those ovules (assuming independence), with a 99% chance that the pollen came from the local subpopulation and a 1% chance that it was carried from the other subpopulation. Finally, we loop to generate seeds for the fertilized ovules, using the proper pollen sources.

This model doesn't show any particularly exciting behavior; it's just a two-subpopulation neutral model with a little gene flow. But it models pollen flow correctly, and thus provides a good foundation for building a more complex model of plant evolution.

Those interesting in modeling plants might also wish to look at the recipe in section 11.3, which shows how to model gametophytic self-incompatibility. That recipe enforces self-incompatibility with a `modifyChild()` callback, which ought to be compatible with this nonWF model. Note, however, that in nonWF models suppression of a proposed child by a `modifyChild()` callback is the end of that proposed child; in WF models, SLiM loops until the set subpopulation size is filled, but in nonWF models SLiM simply attempts to generate each requested offspring, and those that are rejected by a `modifyChild()` callback are abandoned. That behavior might be realistic and desirable (if pollen limitation is severe, or if stigmas are getting clogged by a large amount of incompatible pollen that prevents fertilization); if not, if is easy enough to make the `reproduction()` callback loop until offspring generation succeeds. (The `addCrossed()` method will return `NULL` if the requested offspring is not generated.) Alternatively, one could implement the self-incompatibility system directly in the `reproduction()` callback, rather than in a `modifyChild()` callback, ensuring that the flower chosen as a pollen source for each fertilized ovule is compatible. The latter approach is perhaps simpler, and should be faster.

15.9 Litter size and parental investment

Litter size (clutch size, brood size) is often involved in evolutionary trade-offs. All else being equal, a larger litter is obviously better; the more offspring, the higher the fraction of one's own genes will be in the next generation. But all else is never equal, because each offspring requires an investment of some sort – at least the energy required to make the egg and sperm, and often quite a bit more beyond that. Offspring that receive insufficient parental investment will suffer lower fitness, and at some point the disadvantages of that, in higher offspring mortality and/or lower offspring mating success, will outweigh the advantages of having the extra offspring. In some species, particularly those in harsh and extreme environments, scraping together enough resources to produce even a single offspring is difficult, and the optimum may lie around one offspring per breeding season or even less; other species pursue a strategy of extremely low parental investment and produce as many offspring as they can. These different life history strategies can sometimes be simplified (or oversimplified) into "*K* strategists" and "*r* strategists"; more broadly, life-history tradeoffs are clearly of central importance in evolutionary biology.

In this recipe we will simulate a species with a quantitative trait that governs its litter size. Section 15.3's recipe included litter size variation, but here it will be governed by genetics, not just chance. We will also account for parental investment and the resulting impact of larger litter size on offspring fitness due to limited parental resources. The `initialize()` callback:

```
initialize() {
    initializeSLiMModelType("nonWF");
    initializeSex("A");
    defineConstant("K", 500);

    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;
    initializeMutationType("m2", 0.5, "n", 0.0, 0.3);  // QTL

    initializeGenomicElementType("g1", c(m1,m2), c(1.0,0.1));
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);
}
```

This is a sexual nonWF model, with both neutral mutations (m1) and QTL mutations (m2). This initialization is probably rote by now.

Moving on to the `reproduction()` callback:

```
reproduction(NULL, "F") {
    mate = subpop.sampleIndividuals(1, sex="M");

    if (mate.size())
    {
       qtlValue = individual.tagF;
       expectedLitterSize = max(0.0, qtlValue + 3);
       litterSize = rpois(1, expectedLitterSize);
       penalty = 3.0 / litterSize;

       for (i in seqLen(litterSize))
       {
          offspring = subpop.addCrossed(individual, mate);
          offspring.setValue("penalty", rgamma(1, penalty, 20));
       }
    }
}
```

This callback applies only to females (the `"F"` in its declaration). The focal female chooses a male mate using `sampleIndividuals()`, and assuming that succeeds (i.e., there is at least one male in the population), the female will generate a litter with that mate. The script gets the female's litter-size phenotype from the `tagF` property where it will be stored (as we will see below) and derives an expected litter size from its value such that the new individuals at the beginning of the simulation, with no QTL mutations, have an expected litter size of `3`. We then calculate the actual litter size by doing a Poisson draw with the expectation as mean, and calculate a fitness penalty for the offspring based upon the litter size they come from. The initial litter size of `3` entails no fitness penalty, but larger litter sizes will have correspondingly larger penalties because of the decreased amount of parental investment per offspring.

Having determined the litter size and the fitness penalty, we then make the litter's offspring in a loop. (Note the use of `seqLen(litterSize)`, which will produce the correct number of loops even if the litter size is zero; using the sequence operator with `1:litterSize` would be incorrect, since a litter size of `0` would generate the sequence `1 0` and the loop would then run twice instead of zero times. Be careful using the sequence operator in such cases!) Each offspring is generated with a call to `addCrossed()`, and then the fitness penalty due to parental underinvestment is set into a key named `"penalty"` on the offspring for later use. Note that the actual penalty for each individual is drawn from a gamma distribution with a mean of the expected penalty; this is a bit gratuitous, probably, but makes the actual penalty somewhat non-deterministic.

Next we create our initial population:

```
1 early() {
    sim.addSubpop("p1", 500);
    p1.individuals.setValue("penalty", 1.0);
}
```

We set the initial fitness penalty on the new subpopulation's individuals to `1.0` (i.e., no penalty, since this is a multiplicative fitness effect).

Now comes an `early()` event that, together with the `reproduction()` callback, really does the bulk of the work in this model:

```
early() {
    // QTL calculations
    inds = sim.subpopulations.individuals;
    inds.tagF = inds.sumOfMutationsOfType(m2);

    // parental investment fitness penalties
    inds.fitnessScaling = inds.getValue("penalty");

    // non-overlapping generations
    inds[inds.age >= 1].fitnessScaling = 0.0;

    // density-dependence, assuming 50% die of old age
    p1.fitnessScaling = K / (p1.individualCount / 2);
}
```

This callback has four parts, as commented. The first part totals the effects of all QTL (`m2`) mutations for all individuals and puts those totals into the `tagF` property of the individuals; the `reproduction()` callback expects to find the total there, as we already saw, and the output code below uses it as well. The second part fetches individual fitness penalty values using the `"penalty"` key and sets them into the `fitnessScaling` property of the individuals to create the desired fitness effect. The third part makes generations non-overlapping in this model, by setting the fitness of all individuals to `0.0` unless they are new juveniles; of course the same life-history tradeoffs apply with overlapping generations too, but having discrete generations makes the model's operation easier to observe. Finally, the fourth part implements density-dependence with the usual use of the `fitnessScaling` property of the subpopulation; here, however, we account for the fact that we have already effectively killed half of the population from old age, to make the final population size be closer to the desired carrying capacity.

OK, since this is a QTL model we need to zero out the fitness effect of the QTL mutations as usual, so that their only fitness effects are indirect:

```
fitness(m2) { return 1.0; }
```

Then we do a little output in each generation, and provide a termination event:

```
late() {
    // output the phenotypic mean and pop size
    qtlValues = p1.individuals.tagF;
    expectedSizes = pmax(0.0, qtlValues + 3);

    cat(sim.generation + ": " + p1.individualCount + " individuals");
    cat(", mean litter size " + mean(expectedSizes));
    catn();
}
20000 late() { sim.simulationFinished(); }
```

The model starts off like this:

```
1: 500 individuals, mean litter size 3
2: 492 individuals, mean litter size 2.99977
3: 485 individuals, mean litter size 2.99929
...
```

The mean litter sizes printed in the output are calculated in the same way as in the `reproduction()` callback. The model starts with the default litter size of 3, and then QTLs start to arise that modify that value. By the end of the model, we're in a fairly different place:

```
19998: 335 individuals, mean litter size 6.95885
19999: 326 individuals, mean litter size 6.95713
20000: 336 individuals, mean litter size 6.95985
```

With these parameter values and configuration, the model tends to equilibrate at a litter size around `6.5` to `7.5`, but the range of outcomes is fairly broad and values as high as `9` or `10` are often seen; apparently the selection on litter size imposed by this model is not terribly strong, so the fitness peak is pretty broad. In any case, somewhere in this vicinity there seems to be a crossover point where the benefit of more offspring is counterbalanced by the decrease in parental investment. In this simple model, that result could probably be calculated analytically, but of course that would be impossible in a more complex model involving other biological realism as well.

One interesting thing to note about the output above is that the population size at the end is much smaller than it was at the beginning. This is because every individual at the end is suffering from a lack of parental investment, and that depresses the population size below the carrying capacity. We don't even need to think about that; it just happens automatically, as an emergent property of the model.

In this recipe, the penalty for each offspring depends upon the size of the litter to which the offspring belonged. This makes sense when parental investment is, in fact, per offspring, such as feeding newly hatched juveniles in a nest. In other cases, investment might depend upon the expected litter size, not the actual litter size; if a bird adds body fat before the breeding season and uses that energy to generate a predetermined number of eggs, but only a subset of those eggs hatch, the investment is per egg, not per hatched chick. We can modify the recipe for that case by changing the penalty calculation to be:

```
        penalty = 3.0 / expectedLitterSize;
```

Interestingly, even though `litterSize` is drawn from a distribution with a mean of `expectedLitterSize`, this produces fairly different outcomes. The equilibrium litter size reached is now typically around `3.5` to `4.0` – much smaller.

This model has a lesson that goes far beyond litter size and parental investment: nonWF models can include genetic variation, and evolution, of traits that it is difficult or impossible to model in such a way in WF models. One could easily write a nonWF model of the evolution of the sex ratio, or of the selfing or cloning rate, or of migration or dispersal behavior, or of – as here – litter size or parental investment. WF models can include all of those phenomena, but since they are handled by SLiM's core engine in WF models, it is quite difficult to include individual, genetically-based variation in them.

15.10 Spatial competition and spatial mate choice in a nonWF model

In chapter 14 a variety of spatial models were explored, all of which were WF models. Those spatial modeling techniques work just as well in nonWF models – indeed, better in some ways, as we will see. The model here is derived from the recipe of section 14.5, and includes both spatial competition and spatial mate choice.

Let's begin with the `initialize()` callback as usual:

```
initialize() {
    initializeSLiMModelType("nonWF");
    initializeSLiMOptions(dimensionality="xy", periodicity="xy");
    defineConstant("K", 300);   // carrying capacity
    defineConstant("S", 0.1);   // spatial competition distance
```

```
        initializeMutationType("m1", 0.5, "f", 0.0);
        m1.convertToSubstitution = T;

        initializeGenomicElementType("g1", m1, 1.0);
        initializeGenomicElement(g1, 0, 99999);
        initializeMutationRate(1e-7);
        initializeRecombinationRate(1e-8);

        // spatial competition
        initializeInteractionType(1, "xy", reciprocal=T, maxDistance=S);

        // spatial mate choice
        initializeInteractionType(2, "xy", reciprocal=T, maxDistance=0.1);
    }
```

We set up "xy" dimensionality with periodic boundary conditions for both dimensions, in order to get a toroidal space (see section 14.12). We will still need density-dependent population regulation of some kind, but since this is a continuous-space model our concept of density ought to depend upon *local* density, not overall population size; K is the carrying capacity that we will aim for by calibrating our local density function. We also define the maximum spatial competition distance with the symbol S. We set up a neutral model with the usual boilerplate code, and initialize spatial interactions for competition and mate choice.

Next let's look at reproduction:

```
    reproduction() {
        // choose our nearest neighbor as a mate, within the max distance
        mate = i2.nearestNeighbors(individual, 1);

        for (i in seqLen(rpois(1, 0.1)))
        {
           if (mate.size())
              offspring = subpop.addCrossed(individual, mate);
           else
              offspring = subpop.addSelfed(individual);

           // set offspring position
           pos = individual.spatialPosition + rnorm(2, 0, 0.02);
           offspring.setSpatialPosition(p1.pointPeriodic(pos));
        }
    }
```

We use interaction i2 to find a mate within the maximum mating distance. If one is found, addCrossed() is used for biparental mating, otherwise addSelfed() is used for selfing (note this variation in individual mating behavior based on spatial dynamics, which would be quite difficult to achieve in a WF model). In either case, we draw a litter size using rpois() with an expected mean size of 0.1, so individuals will reproduce relatively infrequently and generations will be highly overlapping; if we're at equilibrium and a new individual is born from a given parent 10% of the time, then individuals ought to have an average lifespan of 10 generations. We loop over our litter size (note the use of seqLen(), so that if the litter size is zero we get the correct behavior; using 1:rpois() instead would yield the sequence 1 0 when the litter size is zero, erroneously producing two offspring). Each offspring is positioned a small distance from the first parent, with accounting for the periodic boundaries.

Population initialization is very similar to the WF model:

```
1 early() {
    sim.addSubpop("p1", 1);

    // random initial positions
    for (ind in p1.individuals)
       ind.setSpatialPosition(p1.pointUniform());
}
```

Note that because individuals that can't find mates self, we can start the model with just a single individual and let it grow to capacity. Next we have spatial competition:

```
early() {
    i1.evaluate();

    // spatial competition provides density-dependent selection
    inds = p1.individuals;
    competition = i1.totalOfNeighborStrengths(inds);
    competition = (competition + 1) / (PI * S^2);
    inds.fitnessScaling = K / competition;
}
```

We evaluate `i1`, and then we evaluate the effect of competition for all individuals in a vectorized fashion. The call to `totalOfNeighborStrengths()` returns a vector of the interaction strength felt by each individual, and we rescale these values to normalize them (discussed below). The fitness effect on each individual is then calculated as the carrying capacity `K` divided by the rescaled strength of competition felt by the individual. If that strength is equal to `K`, we are at equilibrium; the individual will feel no fitness effect, positive or negative, from spatial competition. If the local population density around the individual is higher than that equilibrium density, its fitness will be lower, and vice versa; *local* density is what is actually enforced by this formula, not total population size. If the population happens to be uniformly distributed in space, then its equilibrium size will be equal to `K`; but if there are areas of space that are uninhabitable, or if individuals tend to cluster for whatever reason, then the equilibrium population size may be different from `K`.

To understand how the rescaling works, it is useful to imagine that the maximum competition distance, `S`, is set such that the circle covered by the interaction radius around a focal individual has an area of exactly `1.0`. The term `(PI * S^2)` is the area of this interaction circle, so in this case it would be `1.0`. The focal individual's interaction circle would then include every individual in the model (since the area of the space defined by `p1` is also `1.0`, since we didn't change its dimensions from a unit square; if we had, this formula would need to be tweaked accordingly). The value of competition will thus be the population size, minus one because the focal individual is not itself included in the total interaction strength; we compensate by using `(competition + 1)`. For our hypothetical situation in which the interaction circle has area `1.0`, it can thus be seen that the fitness scaling value for every individual will be exactly `1.0` when the population is at carrying capacity. The same logic applies for other values of `S` – except for the caveat above that a non-uniform spatial distribution might lead to a different equilibrium population size.

Finally, note that periodic boundary conditions are important when modeling competition in this sort of way, because they provide a uniform strength of competition across space, without edge effects. With any non-periodic boundary condition, the strength of spatial competition felt by individuals at the edge of the space will be lower, and that will encourage the population density to be higher at the edges than in the center (because, in effect, the local population density being regulated by the competition function includes the empty areas beyond the edges of the space).

So far so good. Since we have overlapping generations, it would be nice to model some movement by the individuals in the model, rather than just representing them as motionless points. To do that, we have a `late()` event that moves everybody around:

```
late()
{
    // move around a bit
    for (ind in p1.individuals)
    {
       newPos = ind.spatialPosition + runif(2, -0.01, 0.01);
       ind.setSpatialPosition(p1.pointPeriodic(newPos));
    }

    // then look for mates
    i2.evaluate();
}
```

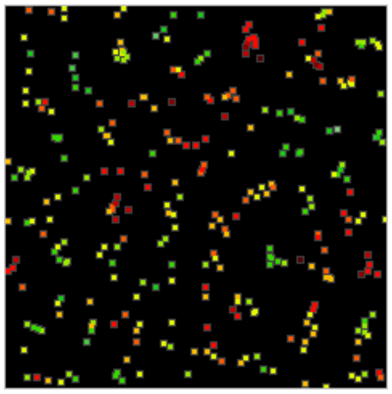
This just deviates individual positions by a small random factor, with accounting for periodic boundaries. After doing that, it evaluates `i2` in preparation for the mate-searching that will occur in `reproduction()` callbacks at the start of the next generation; this just happens to be a convenient moment for that evaluation, right after final positions for the generation have been established.

Finally, we have a termination event:

```
10000 late() {
    sim.outputFixedMutations();
}
```

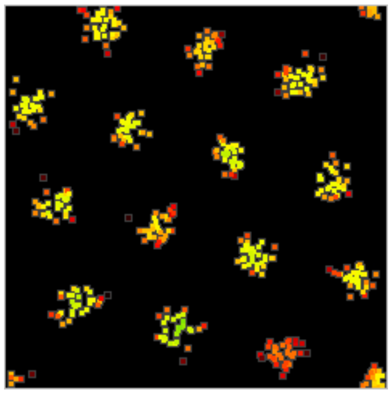
Something worth noting about this model is that it contains no `modifyChild()` callback. Because nonWF models create their own offspring, we can fix the spatial positions of offspring directly in the `reproduction()` callback. It would also work to do it in a separate `modifyChild()` callback, as in section 14.5, but that would be a bit more complex and a bit slower. Similarly, notice that this model contains no `fitness(NULL)` callback, even though spatial competition modifies individual fitness values in the model, because we can use the `fitnessScaling` property of the individuals to implement the fitness effect. Often, nonWF models can get away with fewer callbacks, or even no callbacks except `initialize()` and `reproduction()`, as shown here.

When this recipe is run, it looks a lot like the recipe from section 14.5:



There are differences from section 14.5's recipe, though: individuals are moving around in space during their lifetimes, and generations are clearly overlapping; there is much more continuity from generation to generation. The population size is no longer fixed at `K`, either; it starts at `1` and grows organically, with a natural pattern of population growth that spreads across space. Even once it reaches carrying capacity it is not fixed at exactly `K`, as the WF model was, but fluctuates around the carrying capacity stochastically, depending in part upon how non-uniform the spatial clustering at any given moment happens to be. This added realism could be very important in some models. For example, if something were to suddenly perturb the population – if a disease outbreak in one corner of the space suddenly killed off all the individuals within a small radius, say – the WF model would nevertheless force the total population size to be `K` in every generation, and so the population density would increase in all the other areas of the space, which clearly makes no sense. This model's more robust implementation of population regulation based upon local population density prevents that aberration; the population size would initially be depressed by the perturbation, and the hole created by the disease outbreak would fill back in from its edges naturally, over time.

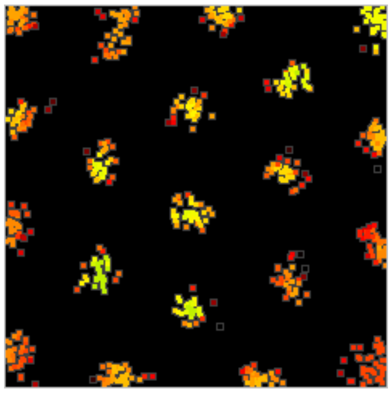
It has been mentioned several times now that spatial clustering might cause this model to reach an equilibrium population size different from `K`. In the snapshot above, it is not immediately obvious that this is happening, but in fact it is, and the population size of this recipe fluctuates around roughly `310`, slightly above the intended carrying capacity of `300`. This can be made much more obvious by increasing `S` to `0.2`; the model at equilibrium then looks like this:



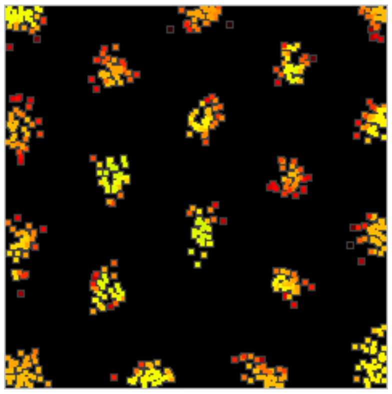
Rather remarkably, the population has naturally clustered itself into fifteen clumps, equidistantly arranged across the periodic space in a hexagonal pattern; this seems to be the optimal arrangement for this value of `S`, and the model finds it fairly quickly every time it is run. The equilibrium population size is now about `500` individuals. In the next section, we will discuss this phenomenon further, and look at a way of preventing it if it is undesirable.

For now, let's just note that this is not a bug; this is the emergent behavior of the model, and it is not necessarily unbiological. For one thing, some species are territorial, and what this model is doing could be seen as a sort of territoriality; if the carrying capacity were adjusted appropriately, each cluster could contain the appropriate number of individuals for family groups of the modeled species. For another, complex spatial clustering has been observed in various natural systems; Vincenot et al. (2016) provide an overview of some examples in plants, for instance, and discuss the modeling of such clustering. Of course these clusters might not behave precisely as one might wish; they are probably almost completely genetically isolated from each other, for one thing, so one might wish to model dispersal that would provide gene flow (such as the way that young male lions leave their natal pride and head out to form their own pride, if they can).

There is one more interesting aside to be explored here. We can modify this recipe a bit more, by removing the periodic boundaries and instead implemented reprising boundaries following the appropriate recipe from section 14.3. With `S` still set to `0.2`, if we run this modified model we will see a fairly different pattern of spatial clustering:



Twelve clusters are now arranged around the edges, and another eight clusters are packed into the interior in an asymmetrical pattern. This is one way that the model can satisfy the constraints it has been given, but it is not entirely stable, and there are several other configurations with either nineteen or twenty clusters that are commonly observed. Here is another, with nineteen:



The equilibrium population size here is about `680` in the top configuration, and about `660` in the bottom configuration. This is higher than it was with periodic boundaries, and of course the nineteen or twenty clusters observed now is more than the fifteen observed with periodic boundaries too. This difference is because reprising boundaries provide the model with more elbow room; the clusters can now take advantage of the fact that they feel no competition from the empty space beyond the edges, whereas periodic boundaries did not afford this luxury.

The overall point, then, is that spatial models are considerably more subtle than one might initially appreciate, and that choices such as boundary conditions can have large consequences for dynamics that might not be immediately obvious. In the next section we shall explore this further.

15.11 A spatial model with carrying-capacity density

The previous section provided a recipe for a nonWF model with both spatial competition and spatial mate choice. Spatial competition provided population regulation, since more individuals would produce more competition, reducing absolute fitness. However, as we saw at the end of the section, that model tends to produce spatial clustering that might be undesirable. This occurs because of the shape of the competition function. The competitive interaction strength felt between two individuals in that recipe was constant out to the maximum interaction distance, and then fell off abruptly to zero. This produces an incentive for clustering, for two reasons: (1) being tightly clustered implies no more fitness penalty than being loosely clustered, since the interaction strength is constant, and (2) clustering allows the empty spaces between clusters to be shared; if the clusters arrange themselves into a regularly spaced configuration, they can efficiently share the empty spaces between them. That effect allows the mean interaction strength felt by individuals to decrease, in turn allowing the model to somewhat exceed its carrying capacity.

For this reason (and others), a Gaussian competition kernel is often preferred in this sort of spatial model; it seems to produce fewer artifacts of this type. In chapter 14 we constructed a series of models inspired by classic papers such as Dieckmann & Doebeli (1999) and Doebeli & Dieckmann (2003), and here we return to that thread. Doebeli & Dieckmann (2003) introduced a concept that they called "carrying-capacity density", based upon a Gaussian competition kernel; with the proper scaling, as set out in their paper, the population will equilibrate at the intended carrying capacity if the environment is homogeneous, just as it did in the previous recipe, but clustering artifacts driven by the shape of the competition kernel will be minimized. Here, we will adjust the model of section 15.10 to implement this concept of carrying-capacity density, which requires only a few minor modifications. Since the modifications are small, we will here review only the sections of the model that are changed (as usual, the full recipe is available in SLiMgui and online).

One part that requires changes is the `initialize()` callback:

```
initialize() {
    initializeSLiMModelType("nonWF");
    initializeSLiMOptions(dimensionality="xy", periodicity="xy");
    defineConstant("K", 300);   // carrying-capacity density
    defineConstant("S", 0.1);   // sigma_S, the spatial competition width

    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;

    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);

    // spatial competition
    initializeInteractionType(1, "xy", reciprocal=T, maxDistance=S * 3);
    i1.setInteractionFunction("n", 1.0, S);

    // spatial mate choice
    initializeInteractionType(2, "xy", reciprocal=T, maxDistance=0.1);
}
```

We now call `K` the carrying-capacity density, and `S` the spatial competition width, which is referred to with the symbol σ_S in Doebeli & Dieckmann (2003). The spatial competition function now uses a Gaussian kernel (type `"n"`), with a maximum distance of three standard deviations (so by the time it cuts off it should be very close to zero anyway). Otherwise this initialize() callback is the same as in section 15.10.

The other element that changes is the population regulation event:

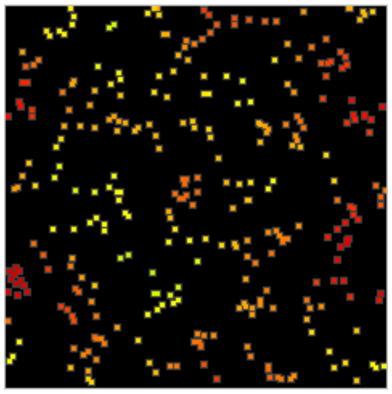
```
early() {
    i1.evaluate();

    // spatial competition provides density-dependent selection
    inds = p1.individuals;
    competition = i1.totalOfNeighborStrengths(inds);
    competition = competition / (2 * PI * S^2);
    inds.fitnessScaling = K / competition;
}
```

This is quite similar to section 15.10's code, but the rescaling of the competition strength has changed in accord with the new Gaussian competition kernel shape. The new rescaling is parallel to the rescaling that is applied in the standard formula for the normal distribution:

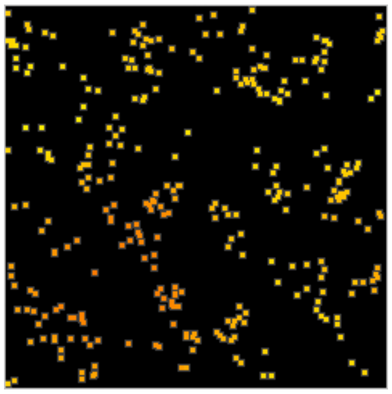
$$f(x \mid \mu, \sigma^2) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(x-\mu)^2}{2\sigma^2}}$$

Without the rescaling constant, that formula would produce a maximum value of `1.0`; rescaled, it produces a lower maximum density, such that the total probability density – the integral under the curve – is exactly `1.0` (as required by the definition of a probability density function). Now, note that the Gaussian interaction function we're using here utilizes the same formula, but without that rescaling factor; we just want to introduce that rescaling factor to normalize the Gaussian interaction function. This is parallel to the reasoning followed in section 15.10 that led us to rescale using the formula for the area of a circle of radius `S`. The rescaling factor is squared in this recipe (no square root) because we have two spatial dimensions; the spatial competition function is really the product of two Gaussian functions, one for *x* and one for *y*. See Doebeli & Dieckmann (2003) and related papers, from which this mathematical framework is derived, for further discussion, since a full derivation is beyond the scope of this manual. Note that, in terms of implementation, we could just rescale the maximum strength for `i1` instead, supplying the same rescaling constant directly to `setInteractionFunction()`, and that would run faster, too; the design shown here is more explicit for pedagogical purposes.

When this recipe is run, it looks a lot like the recipe from section 14.10:



Close examination, however, shows that this spatial distribution is less regularly clustered than that previous recipe's distribution. Changing `S` to `0.2` shows that the clustering previously observed at that interaction scale is all but gone too:



A little bit of clustering still occurs, partly because offspring land near their first parent, and partly just as a result of stochasticity (one would not expect a stochastic process to produce a perfectly uniform spatial distribution, after all). But the competition function is no longer contributing heavily to that clustering as it was before; indeed, it may be working to smooth it away by favoring new offspring that land in relatively unoccupied areas.

Incidentally, these effects of interaction kernel shape have been explored in various papers; see Payne et al. (2011) for a model of this based upon the same Dieckmann and Doebeli models that we have been exploring, although that paper concerns itself more with clustering in phenotypic space than in the regular spatial dimensions (as we saw in chapter 14, phenotype can in some ways be treated similarly to a spatial dimension). Payne et al. (2011) found that a box-shaped (i.e., platykurtic) kernel encouraged clustering, just as did the cut-off kernel we used in section 15.10, which was of course also platykurtic. Leimar et al. (2008) explored competition kernel shape in more detail, and found that a characteristic of the Fourier transform of the competition kernel was predictive of its effects upon clustering. A Gaussian competition kernel does not promote clustering, according to their findings, and this is one reason why this kernel shape is popular (although mathematical convenience also plays a role, as they explain).

15.12 Forcing a specific pedigree in a nonWF model

In section 13.7, we saw a recipe for forcing a SLiM model to follow a specific pedigree through arranged matings between individuals. That recipe worked within the WF model framework, which made its task rather difficult, since matings in WF models are arranged by SLiM's core engine. To make it work, that recipe had to reject undesired proposed children with a `modifyChild()` callback, a solution that is slow and scales poorly to larger pedigrees. It was, in short, an exercise in trying to pound a square peg into a round hole.

With a nonWF model we can do much better, since in nonWF models matings are arranged by the model's script, not by SLiM's core engine; in a nonWF model we can simply request the matings we want to get. That is what we will do in this section's recipe. In other respects the approach here is similar to that of section 13.7's recipe; we use the `tag` values of individuals to identify each individual, with a unique value for every individual in the entire pedigree.

This section actually has two recipes in it. The first recipe is for a nonWF model that allows random matings with overlapping generations; it tracks each individual's ancestry and outputs two files that record the population's history. The first output file records the generation in which each individual died (since we are modelling overlapping generations), and the second records every mating event and the identities of the individuals involved.

The second recipe reads those files back in, and reproduces the exact pedigree and population history that occurred during the run of the first recipe. It reproduces death events by setting a fitness of zero for individuals slated to die in a given generation, and it reproduces mating events by calling `addCrossed()` for each pair of individuals slated to mate in a given generation, in the model's `reproduction()` callback.

If you want to reproduce the pedigree followed in a "baseline" model run, these two recipes should allow you to do exactly that, with little modification. If, on the other hand, you have pedigree information from source other source (such as empirical data from a real population), you can use the second recipe to force SLiM to follow that pedigree; you would just need to either encode your pedigree in the file format expected by the recipe, or modify the recipe to read in whatever file format you already have.

So, let's begin with the first recipe, which tracks and outputs the pedigree realized by a model run:

```
initialize() {
    initializeSLiMModelType("nonWF");
    defineConstant("K", 10);

    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);

    // delete any existing pedigree log files
    deleteFile("~/Desktop/mating.txt");
    deleteFile("~/Desktop/death.txt");
}
reproduction() {
    // choose a mate and generate an offspring
    mate = subpop.sampleIndividuals(1);
    child = subpop.addCrossed(individual, mate);
    child.tag = sim.tag;
    sim.tag = sim.tag + 1;

    // log the mating
    line = paste(c(sim.generation, individual.tag, mate.tag, child.tag));
    writeFile("~/Desktop/mating.txt", line, append=T);
}
1 early() {
    sim.addSubpop("p1", 10);

    // provide initial tags and remember the next tag value
    p1.individuals.tag = 1:10;
    sim.tag = 11;
}
early() {
    // density-dependence
    p1.fitnessScaling = K / p1.individualCount;

    // remember the extant individual tags
    sim.setValue("extant", sim.subpopulations.individuals.tag);
}
late() {
    // log out the individuals that died
    oldExtant = sim.getValue("extant");
    newExtant = sim.subpopulations.individuals.tag;
    survived = (match(oldExtant, newExtant) >= 0);
    died = oldExtant[!survived];

    for (indTag in died)
    {
      line = sim.generation + " " + indTag;
      writeFile("~/Desktop/death.txt", line, append=T);
    }
}
100 late() {
    sim.simulationFinished();
}
```

This recipe is quite straightforward; in most respects it follows the typical skeleton of a nonWF model, but with some logging code added in. In the `initialize()` callback we delete any pre-existing log files; the paths for the log files are of course something you are likely to want to customize. The `reproduction()` callback chooses a random mate and calls `addCrossed()` to generate a child, as usual; but it also sets that child up with a unique identifying `tag` value, and appends a line summarizing the mating event to the `mating.txt` log file. The `1 early()` event sets the subpopulation up as usual, and also sets up initial `tag` values for the new individuals; the value of `sim.tag` is used to track the next unused `tag` value in the run. The `early()` event provides density-dependent population regulation, as we have seen in previous nonWF models; it also remembers the `tag` values of all of the extant individuals prior to the survival generation cycle stage, storing that list away in the simulation object using `setValue()`. Finally, the `late()` event compares the post-mortality list of individuals to the pre-mortality list, determines which individuals died, and appends lines representing those deaths to the `death.txt` log file. (This recipe uses `match()`, but one of the Eidos set-theoretic methods like `setDifference()` could probably be used just as easily.) The model ends at the end of generation `100`.

A run of this model produces `death.txt` and `mating.txt` files on the user's desktop (on Mac OS X, at least; the output paths in the recipe may need to be modified on other platforms). The `death.txt` file is simply a series of lines, each of which has a generation and then the `tag` value of an individual that died in that generation, like this:

```
2 2
2 4
2 6
...
3 7
3 19
...
4 20
4 21
...
```

This file records that in generation `2` the individuals with `tag` values `2`, `4`, `6`, etc., died; in generation `3`, individuals with `tag` values `7`, `19`, etc.; in generation `4`, individuals with `tag` values `20`, `21`, etc.; and so forth, through to the end of the run.

The `mating.txt` file is almost as simple; here, each line records a generation, the `tag` values of the first and second parent, and then the `tag` value of the generated offspring:

```
2 1 3 11
2 2 10 12
2 3 2 13
...
3 1 13 21
3 3 20 22
...
4 1 13 30
4 3 22 31
...
```

The first line in this example, for example, specifies that in generation `2` the individuals with `tag` values `1` and `3` mated to produce an offspring individual with `tag` value `11`.

These files, then provide all the information we need to reproduce the full pedigree and population history of the model run. So much for the first recipe; now let's move on to the second recipe and see how it uses these files to force a replication of the logged pedigree:

```
function (i)readIntTable(s$ path)
{
    l = readFile(path);
    t(sapply(l, "asInteger(strsplit(applyValue));", simplify="matrix"));
}

initialize() {
    initializeSLiMModelType("nonWF");
    defineConstant("K", 10);

    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);

    // read in the pedigree log files
    defineConstant("M", readIntTable("~/Desktop/mating.txt"));
    defineConstant("D", readIntTable("~/Desktop/death.txt"));

    // extract the generations for quick lookup
    defineConstant("Mg", drop(M[,0]));
    defineConstant("Dg", drop(D[,0]));
}
reproduction() {
    // generate all offspring for the generation
    m = M[Mg == sim.generation,];

    for (index in seqLen(nrow(m))) {
       row = m[index,];
       ind = subpop.subsetIndividuals(tag=row[,1]);
       mate = subpop.subsetIndividuals(tag=row[,2]);
       child = subpop.addCrossed(ind, mate);
       child.tag = row[,3];
    }

    self.active = 0;
}
1 early() {
    sim.addSubpop("p1", 10);

    // provide initial tags matching the original model
    p1.individuals.tag = 1:10;
}
early() {
    // execute the predetermined mortality
    inds = p1.individuals;
    inds.fitnessScaling = 1.0;

    d = drop(D[Dg == sim.generation, 1]);
    indices = match(d, inds.tag);
    inds[indices].fitnessScaling = 0.0;
}
100 late() {
    sim.simulationFinished();
}
```

Let's walk through how it works. First of all, we define a new function named `readIntTable()` that reads in a text file from a given filesystem path, assumed to be composed of lines of `integer` values, and returns a matrix representing the contents of the file. (Note that this function is supplied separately in the online SLiM-Extras repository, too.) We haven't used matrices much in previous recipes; they are a relatively new feature of Eidos, and work in much the same way as matrices in R do (see the Eidos manual for further discussion). Indeed, we haven't seen many examples of user-defined functions either (again, see the Eidos manual). Without worrying too much about such details, however, if we treat this function as a black box and call it with the path of our `death.txt` file, we get this matrix:

```
     [,0] [,1]
[0,]    2    2
[1,]    2    4
[2,]    2    6
...
```

And for our `mating.txt` file we get this:

```
     [,0] [,1] [,2] [,3]
[0,]    2    1    3   11
[1,]    2    2   10   12
[2,]    2    3    2   13
...
```

The `initialize()` callback of this recipe sets up the model in the usual way (mirroring the setup of the first recipe, which is what one would probably want in most cases). It then calls `readIntTable()` to read in the log files, and retains the resulting matrices as defined constants, `M` and `D`. Finally, it extracts the first column from `M` and `D` (which contains the generations for each logged event) and retains those as constants `Mg` and `Dg`, for simplicity and speed later. So far so good; this is the information the recipe will use to reproduce the logged pedigree.

Next, the `reproduction()` callback executes the pedigree's mating events. It does this by fetching the rows of `M` that refer to the current generation, and looping through those rows to generate each mating event (again, you may wish to refer to the Eidos manual for information on the syntax involved in working with matrices). The `tag` value of the offspring is set according to the logged pedigree as well, so that the new individual will match up with the `tag` values used in the log files. The callback triggers all of the mating events for the generation in a single call, rather than working with the individual supplied to the `reproduction()` callback, so it then disables itself, by setting `self.active` to `0`, ensuring that it is not called again in the current generation (as we saw before in section 15.3).

The `1 early()` event creates the initial subpopulation, as in the first recipe, and sets the `tag` values of individuals in the same way so that both models get the same setup.

Finally, we have the `early()` event. This does not cause density-dependent population regulation in the usual way of nonWF models; instead, it uses the `fitnessScaling` property values of individuals to weed out specifically the individuals that died in each generation in the original model run. It begins by setting `fitnessScaling` to `1.0` on all individuals. Then it looks up the mortality events for the current generation, similarly to how the `reproduction()` callback looked up mating events. It then uses `match()` to find the indices of the individuals in question, and sets `fitnessScaling` to `0.0` for those individuals. Those individuals will be killed by SLiM during the survival generation cycle stage that follows the `early()` event. The model terminates at the end of generation `100`, matching the behavior of the original model.

In this way, this recipe reproduces the saved pedigree, even when a different random number seed is used. If you run the second recipe repeatedly, you will therefore get replicates of the saved pedigree, but with different mutational and recombinational histories and thus different segregating mutations at the end of the runs. Of course you may not wish to take on faith that the pedigree is replicated exactly, so if you wish you can add calls to `catn()` in the appropriate spots to log out each mating and mortality event, to confirm that they follow the pedigree as intended.

This basic scheme could be extended in various ways, as needed. For example, the log files presently support only biparental matings; if you wanted to force a pedigree that involved cloning in some cases, you could extend the `mating.txt` file format to have an extra column with a value indicating whether the offspring was generated by cloning or not, or you could add a third log file, named something like `cloning.txt`, to record those events; either strategy would work. You could also log out, and then reproduce, other model events if you wished, such as migration events; since you are in complete control of such events in nonWF models, doing this would be quite a straightforward extension of these recipes. You could probably even record, and then reproduce, the recombination breakpoints used in the generation of each offspring individual, using a `recombination()` callback, so as to make the replicate run duplicate exactly the same pattern of local ancestry along the chromosome as the original model run, if you wanted to. This strategy, of driving model dynamics from file-based data, is quite general and can be applied to many tasks. It is much cleaner to implement with nonWF models, however, since nonWF models are so much more strongly script-driven than WF models; it would presumably be possible to make section 13.7's recipe file-driven in this manner, but it would scale very poorly to large pedigrees.

15.13 Modeling clonal haploids in a nonWF model with `addRecombinant()`

In section 13.13 we saw a recipe for modeling clonal haploids in SLiM by keeping the second genome of each individual empty. New mutations arising in those second genomes were removed in each generation, and a recombination rate of zero was used to prevent any recombination with those empty genomes. That recipe is general and flexible; as noted there, similar strategies could be employed to model haploid mitochondrial DNA alongside diploid autosomal chromosomes, or to model haplodiploidy and other such systems.

However, that strategy does have some drawbacks, particularly when tree-sequence recording is being used (discussed in detail in chapter 16, but see section 1.7 for a quick introduction). With tree-sequence recording, the recipe of section 13.13 records rather odd dynamics, with mutations appearing and then disappearing in each generation, and the empty second genomes of individuals inheriting from each other. These bizarre inheritance records are probably harmless, but may complicate post-simulation analysis, and in any case constitute something of an offense against clean design. Even more problematic for section 13.13's strategy, when doing tree-sequence recording, is the question of how to model horizontal gene transfer, as we will discuss in section 15.14.

Here, then, we will look at an alternative strategy for modeling clonal haploids. This strategy can be employed only in nonWF models, but integrates much more smoothly with tree-sequence recording and is conceptually more straightforward as well.

The recipe, in full:

```
initialize() {
    initializeSLiMModelType("nonWF");
    defineConstant("K", 500);      // carrying capacity
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);
}
```

```
reproduction() {
    subpop.addRecombinant(genome1, NULL, NULL, NULL, NULL, NULL);
}
1 early() {
    sim.addSubpop("p1", 500);
}
early() {
    p1.fitnessScaling = K / p1.individualCount;
}
late() {
    // remove neutral mutations in the haploid genomes that have fixed
    muts = sim.mutationsOfType(m1);
    freqs = sim.mutationFrequencies(NULL, muts);

    if (sum(freqs == 0.5))
      sim.subpopulations.genomes.removeMutations(muts[freqs == 0.5], T);
}
50000 late() { sim.outputFixedMutations(); }
```

This has the typical nonWF setup and population regulation, as we have seen before. The `late()` event removes neutral mutations (type `m1`) when they reach fixation at a frequency of `0.5`, since SLiM doesn't know enough to do so, following a similar strategy to section 13.13; see that section for discussion.

The interesting and new part of this model is the `reproduction()` callback, which uses a method we have not seen before, `addRecombinant()`. Like `addCrossed()`, `addCloned()`, `addSelfed()`, and `addEmpty()`, this adds a new offspring individual to the target subpopulation, but it provides greater control over precisely how that new individual is generated. Section 21.13.2 provides full documentation on this complex method, but in short, it allows you to supply two parent genomes for each genome in the new offspring, with a list of recombination breakpoints to be used in stitching together those parent genomes through crossover. The first three parameters to its call here specify that genome1 from the focal parent should be used to generate the offspring's first genome, with no second recombinant strand (`NULL`), and no recombination breakpoints (`NULL`); this provides clonal reproduction of the first genome. New mutations will be added by SLiM as usual. The second group of three parameters to `addRecombinant()` are all `NULL` here; that specifies that the second genome of the offspring should be generated with no parent genomes at all, leaving it empty, just as `addEmpty()` would have done. In this case, `addRecombinant()` does not add new mutations to the genome, since conceptually there is no parental genome to mutate.

This approach, using `addRecombinant()`, allows the model to tell SLiM precisely how to generate offspring. This has several benefits. One is that, unlike the recipe of section 13.13, we don't have to go back and remove mutations added by SLiM to the second genomes of individuals; SLiM knows not to add mutations to those genomes in the first place. Another is that tree-sequence recording, if enabled, is able to better understand and record what is going on; it does not record the addition and removal of spurious mutations, and all of the second genomes of individuals in this model will be recorded as having no parents and no descendants, producing a cleaner recorded tree sequence that better reflects the fact that those second genomes do not actually exist at all, conceptually. The third benefit of using `addRecombinant()` is that is allows more complex modes of offspring generation to be expressed as well; as an example, in the next section we will see how to model horizontal gene transfer in bacteria using `addRecombinant()` to express the horizontal gene transfer to SLiM.

15.14 Modeling clonal haploid bacteria with horizontal gene transfer

In section 15.13 we looked at a model of clonal haploids using `addRecombinant()`, as an alternative to the original haploid clonal model presented in section 13.13. The use of `addRecombinant()` allowed the details of child generation to be expressed precisely to SLiM, facilitating a simpler model design and more accurate recording of ancestry in the tree sequence (if tree-sequence recording were enabled; see section 1.7). In this section we'll explore those benefits in more detail in a model of horizontal gene transfer in bacteria.

This is a more complex model than that of section 15.13, so let's take things in two steps. First, here is all of the code except the `reproduction()` callback:

```
initialize() {
    initializeSLiMModelType("nonWF");
    defineConstant("K", 1e5);                      // carrying capacity
    defineConstant("L", 1e5);                      // chromosome length
    defineConstant("H", 0.001);                    // HGT probability
    initializeMutationType("m1", 1.0, "f", 0.0);   // neutral (unused)
    initializeMutationType("m2", 1.0, "f", 0.1);   // beneficial
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, L-1);
    initializeMutationRate(0);                     // no mutations
    initializeRecombinationRate(0);                // no recombination
}
1 early() {
    // start from two bacteria with different beneficial mutations
    sim.addSubpop("p1", 2);

    // add beneficial mutations to each bacterium, but at different loci
    g = p1.individuals.genome1;
    g[0].addNewDrawnMutation(m2, asInteger(L * 0.25));
    g[1].addNewDrawnMutation(m2, asInteger(L * 0.75));
}
early() {
    // density-dependent population regulation
    p1.fitnessScaling = K / p1.individualCount;
}
late() {
    // detect fixation/loss of the beneficial mutations
    muts = sim.mutations;
    freqs = sim.mutationFrequencies(NULL, muts);

    if (all(freqs == 0.5))
    {
       catn(sim.generation + ": " + sum(freqs == 0.5) + " fixed.");
       sim.simulationFinished();
    }
}
1e6 late() { catn(sim.generation + ": no result."); }
```

The `initialize()` code defines a few constants: the carrying capacity, the chromosome length, and the probability that horizontal gene transfer will occur during a given mitosis event. Note that we will model horizontal gene transfer as occurring during reproduction, rather than as a discrete event occurring later in a bacterium's lifetime. This design is much simpler, particularly if tree-sequence recording is enabled; horizontal gene transfer changes the genealogical relationships among individuals, and tree-sequence recording is not designed to accommodate such changes in the middle of an individual's lifespan. The approximation seems unlikely to matter.

Note also that although we define a neutral mutation type here, `m1`, we do not model neutral mutations, and indeed, we use a mutation rate of `0.0`. This is because a model of this sort is likely to use tree-sequence recording to overlay neutral mutations after the fact for much greater speed; since we haven't gotten into tree-sequence recording yet, however, we will defer that topic until sections 16.1 and 16.2. For now, it suffices to say that we do not model neutral mutations here.

The initial population here consists of just two bacteria, which are set up to carry different beneficial mutations at different locations in the genome. The population will expand exponentially until reaching the carrying capacity of `1e5`. We have used a fairly large population size since we are modeling bacteria, but a carrying capacity of `1e6` or even higher might be desirable for some purposes. Apart from taking more time and memory, this model should scale up without difficulties; the fact that neutral mutations are not included makes it scale much better.

In the `late()` event we detect the fixation or loss of the beneficial mutations; if both mutations have fixed or been lost, the model prints a message indicating how many mutations fixed, and then stops. If the model runs for `1e6` generations without fixation or loss, it stops with a diagnostic message.

All of that is fairly routine. Now here's the `reproduction()` callback, where the interesting action happens:

```
reproduction() {
    if (runif(1) < H)
    {
        // horizontal gene transfer from a randomly chosen individual
        HGTsource = p1.sampleIndividuals(1, exclude=individual).genome1;

        // draw two distinct locations; redraw if we get a duplicate
        do breaks = rdunif(2, max=L-1);
        while (breaks[0] == breaks[1]);

        // HGT from breaks[0] forward to breaks[1] on a circular chromosome
        if (breaks[0] > breaks[1])
            breaks = c(0, breaks[1], breaks[0]);

        subpop.addRecombinant(genome1, HGTsource, breaks, NULL, NULL, NULL);
    }
    else
    {
        // no horizontal gene transfer; clonal replication
        subpop.addRecombinant(genome1, NULL, NULL, NULL, NULL, NULL);
    }
}
```

Each bacterium reproduces exactly once each generation, producing two bacteria from one, which makes sense from the perspective of reproduction by mitosis. This reproduction can happen in two different ways, depending upon a random draw from `runif()`. If the draw is greater than or equal to `H`, reproduction is purely clonal as in the model of section 15.13; that is the `else` clause here. If the draw is less than `H`, horizontal gene transfer occurs, which needs some explanation.

In that case, we first draw a random individual (other than the focal individual) to act as the source for the transfer, and get its first genome. Next we use a `do–while` loop to draw two distinct locations along the genome; these will be the endpoints of the transfer. Specifically, the transfer will start at `breaks[0]` and go forward to `breaks[1]`. For a bit of extra biological realism, we will model a circular chromosome here, so if `breaks[0]` is greater than `breaks[1]` the transfer will wrap around from the end of the genome to the start, as modelled in SLiM; we check for that case and patch up the breaks vector to reflect what we want to happen in that situation. Finally, we call `addRecombinant()` to generate the offspring bacterium including the horizontal gene transfer. We pass it to the parent genomes – that of the reproducing bacterium, and that of the horizontal gene transfer source – with the breakpoint vector that describes when SLiM should switch between those strands as it produces the offspring genome by recombination. As before, we pass `NULL` for the next three parameters to indicate that the second offspring genome should be empty. (A diploid model that wanted to generate its own recombination breakpoints might use those parameters, for example.)

Without horizontal gene transfer, this would be a model of clonal competition: one lineage would end up "winning" and the other would go extinct, although it might take a long time for that outcome to be reached since it would depend on drift. This behavior can be seen by setting the defined constant `H` to `0.0`. With horizontal gene transfer, however, the bacteria will often stumble upon a lineage (or perhaps more than one lineage) that combines both mutations in the same genome, providing them with an advantage similar to that provided by recombination in sexual reproduction. Once such a lineage arises it will almost always win, and we will get output like this from the model:

```
197: 2 fixed.
```

Both beneficial mutations fixed in generation 197, thanks to horizontal gene transfer.

The details of the breakpoint generation here might need to be modified in a more realistic model. Here we draw the start and end positions of the transfer region independently, but perhaps it would be better to draw the start location randomly and then draw a transfer length from a geometric distribution or some other distribution. This would constrain the horizontal gene transfer to generally be a small minority of the genome, as is typical in the transfer of a plasmid or a transposon. The location and length of the transfer could also be constrained by some sort of genetic structure to explicitly model the transfer of a plasmid that spans a given range of the genome, of course. The `reproduction()` callback could also base the choice of whether or not horizontal gene transfer occurs upon the contents of the two genomes in question, not just upon a random probability; one could model a selfish gene in the transfer donor that makes horizontal gene transfer more likely to occur, for example. Since all of the logic governing the horizontal gene transfer is in the model's script, it can include whatever biological realism is of interest.

Note that prior to the addition of `addRecombinant()` in SLiM, it would have been possible to model horizontal gene transfer by actually getting all of the mutations from the transfer region out of the source's genome, and then adding them into the target's genome with `addMutations()` (removing any existing mutations from the target region first). This would work fine except that it obscures what is actually going on in terms of genealogy and inheritance. If tree-sequence recording were used with such a model, the transferred region would not be recorded as originating in the source genome; instead, the mutations would just magically appear in the target genome, with no genealogical relationship between source and target recorded in the tree sequence. The method presented here, using `addRecombinant()`, is therefore preferable. (If one needed to model even more complex patterns of inheritance – offspring genomes that consist of a mosaic of genetic material from more than two parental genomes, for example – using the `addMutations()` technique might still be necessary, however, since `addRecombinant()` is designed to record at most two parental genomes for each offspring genome. Tree-sequence recording would not work well in such a model, however.)

To make a relatively realistic models of bacterial evolution with SLiM, this sort of realistic inheritance and horizontal gene transfer is one important ingredient. The other important ingredient is the ability to make models with a sufficiently large population size, which is made possible by the enormous performance benefits provided by tree-sequence recording as we will see in chapter 16.

15.15 Implementing a Wright–Fisher model with a nonWF model

In this chapter, we have focused on the aspects of nonWF models that go beyond the Wright–Fisher model, such as overlapping generations, age structure, and individual-level control over events such as reproduction and migration. Sometimes, however, it can be useful to implement a Wright–Fisher model as a nonWF model in SLiM – or at least some aspects of a Wright–Fisher model. You might want to have discrete, non-overlapping generations, for example; or you might want panmictic offspring generation as in the Wright–Fisher model, with each offspring being generated from an independent, randomly drawn pair of parents. Implementing such a model using the nonWF model type might still be desirable, because you might also want some non-Wright–Fisher dynamics in your model that would be difficult to implement in a WF model in SLiM, or you might want to take advantage of certain features of SLiM that are only available in nonWF models (such as the `addRecombinant()` method used in the previous two sections). In this section, then, we will build a nonWF model that incorporates most aspects of the Wright–Fisher model.

The recipe here is quite simple, so we will look at it in full:

```
initialize() {
    initializeSLiMModelType("nonWF");
    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8);
}
reproduction() {
    K = sim.getValue("K");
    for (i in seqLen(K))
    {
       firstParent = p1.sampleIndividuals(1);
       secondParent = p1.sampleIndividuals(1);
       p1.addCrossed(firstParent, secondParent);
    }
    self.active = 0;
}
1 early() {
    sim.setValue("K", 500);
    sim.addSubpop("p1", sim.getValue("K"));
}
early()
{
    inds = sim.subpopulations.individuals;
    inds[inds.age > 0].fitnessScaling = 0.0;
}
10000 late() { sim.outputFixedMutations(); }
```

In the `initialize()` callback, we set up this simple nonWF model with neutral mutations and a uniform chromosome as usual. Note that we do not set up a constant `K` for the population carrying capacity there; instead, in the `1 early()` event, we set `K` up as a value kept by the simulation using `setValue()`, making it easier to vary `K` over time (although we don't do so in this simple recipe). The `p1` subpopulation begins with a size equal to the value of `K` just defined.

The `reproduction()` callback implements a Wright–Fisher style of reproduction. It gets the current subpopulation size using `getValue()`, and then generates that many offspring into `p1` with randomly drawn parents for each offspring. It then deactivates itself by setting `self.active` to `0`, to prevent SLiM from calling it again, since it has reproduced the entire subpopulation; we first saw this strategy in section 15.3. Note that this code does not prevent `firstParent` and `secondParent` from being the same individual, so a certain amount of "incidental selfing" will occur (as is typical in the Wright–Fisher model); it would be easy to fix that with this revised line:

```
    secondParent = p1.sampleIndividuals(1, exclude=firstParent);
```

This draws the second parent from `p1` while explicitly excluding `firstParent` as a choice; the `sampleIndividuals()` method has many useful options of this sort. Changing this model to be sexual instead of hermaphroditic would also be easy, since `sampleIndividuals()` can similarly be told to draw only females (for the first parent) or only males (for the second). One could also easily implement Wright–Fisher style migration between subpopulations by generating some fraction *m* of the new offspring in `p1` from parents drawn from a different subpopulation instead.

The `early()` event implements non-overlapping generations by simply killing off all non-juvenile individuals, by setting their `fitnessScaling` to `0.0`. This is, in effect, an extremely simple version of the sort of life table we saw in section 15.2. Note that unlike most nonWF models, this model has no other population regulation; the usual density-dependence code is absent. Since the `reproduction()` callback always generates exactly `K` offspring, and all non-juveniles are killed off each generation, the size of the population is deterministic and does not require further regulation.

This model remains non-Wright–Fisher in one key way: fitness is still expressed through pre-mating mortality, not through an individual's probability of mating. This has two important consequences. First of all, if the model were changed to be non-neutral – with deleterious mutations, in particular – then the population size would be `K` after offspring generation, but would drop below `K` during the viability/survival generation cycle stage due to fitness-based mortality. The model would thus be a "hard selection" model, not a "soft selection" model as is typical for Wright–Fisher models. Second, the distribution of fecundity among individuals here is different from that of a Wright–Fisher model; in this model, as in most nonWF models, either an individual survives (in which case it has the same expected fecundity as any other surviving individual) or it dies (in which case it has an expected fecundity of zero, being dead). In the Wright–Fisher model, on the other hand, fitness modifies the probability that an individual will be chosen as a mate, and so the distribution of fecundity is continuous rather than bimodal. The fact that fitness influences mortality in nonWF models is an assumption built into SLiM's core code, and would not be easy to change in script; one would have to do a complete end-run around SLiM's built-in fitness calculations. If this difference from the Wright–Fisher model presents a problem, the WF model type probably ought to be used. In many cases, however, the difference may be unimportant.

The other big differences, of course, are that the script for this model is much more complex than the script for the equivalent WF model, and it runs several times slower – about 4×, in an informal test. The speed penalty for switching to a nonWF model is large here because all this model really does is reproduce, and the reproduction for the nonWF model is handled in script rather than in SLiM's core as it is for the WF model. The penalty associated with switching to nonWF is therefore maximized here; if the model had other things to do besides reproduce, the penalty would be smaller. For example, if the chromosome length in this model were 10^7 instead of 10^5, SLiM would spend much more time handling the genetics of the model – doing mutation and recombination, as well as checking for fixation or loss of mutations – and in that case, this recipe would take only 1.35× as long as the equivalent WF model. With a chromosome length of 10^8, the slowdown is only a factor of 1.07×. This underlines that when making the choice between a WF and a nonWF model, that choice should almost always be made based upon which model type is a better fit for the scenario being simulated, rather than upon performance. If a model is big and complex enough that its runtime is problematic – i.e., is measured in hours to days – the overhead due to choosing the nonWF model type will probably be small.

15.16 Alternation of generations

SLiM is generally a framework for modeling diploid organisms, but with some creative scripting that assumption can be modified. We have seen some recipes for modeling haploids, as in sections 13.13, 15.13, and 15.14. In nonWF models a similar strategy can be used to fully model the phenomenon of *alternation of generations*, the way that diploid and haploid life cycle stages generally alternate in organisms that are often thought of simply as "diploids". Many sexual animals, for example, have a multicellular diploid phase that produces a unicellular haploid phase – sperm and eggs – that then fuse, in fertilization, to produce the next diploid generation. In plants this situation is generally even more pronounced, often with a multicellular haploid phase, the gametophyte, that can be free-living and large – often larger and more obvious than the diploid sporophyte, which is often reduced. For many organisms, then, it may be important to model both the haploid and diploid phases explicitly; mutations may be expressed differently between them, selection may act differently upon them, they may migrate or disperse differently, and so forth. SLiM does not have intrinsic support for modeling this alternation of generations, but it is straightforward to implement in script in a nonWF model, as we will see in this section.

This model will be somewhat complicated, so let's start with the setup:

```
initialize()
{
    defineConstant("K", 500);     // carrying capacity (diploid)
    defineConstant("MU", 1e-7);   // mutation rate
    defineConstant("R", 1e-7);    // recombination rate
    defineConstant("L1", 1e5-1);  // chromosome end (length - 1)

    initializeSLiMModelType("nonWF");
    initializeSex("A");
    initializeMutationRate(MU);
    initializeMutationType("m1", 0.5, "f", 0.0);
    m1.convertToSubstitution = T;
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, L1);
    initializeRecombinationRate(R);
}
1 early()
{
    sim.addSubpop("p1", K);
    sim.addSubpop("p2", 0);
}
```

We use defined constants for several of the model parameters in this recipe. The recipe here involves only neutral mutations, but extending it to other types of mutations should present no difficulties.

This is a sexual model, so we set up separate sexes with `initializeSex()`. We are not modeling sex chromosomes, but we will track the sex of individuals in both the diploid and haploid phase; sperm will be considered "male", and eggs "female", in this model.

A key point in the design of this model is that although we are modeling only a single subpopulation, we use two subpopulations in the model, `p1` and `p2`. The first, `p1`, is used to hold diploids; the second, `p2`, is used to hold the haploid sperm and eggs. This separation is not strictly necessary, but it makes the design of the model simpler, because this way we can define a `reproduction()` callback for `p1` that reproduces the diploids (producing sperm and eggs), and a separate `reproduction()` callback for `p2` that reproduces the haploids (producing fertilized eggs that develop into diploids). For other processing of the individuals in the model, such as `fitness()` callbacks, this partitioning will also prove useful, as we will see below.

The next step is to define the `reproduction()` callbacks. Let's start with the one for `p1`:

```
reproduction(p1)
{
    g_1 = genome1;
    g_2 = genome2;
    
    for (meiosisCount in 1:5)
    {
      if (individual.sex == "M")
      {
        breaks = sim.chromosome.drawBreakpoints(individual);
        s_1 = p2.addRecombinant(g_1, g_2, breaks, NULL, NULL, NULL, "M");
        s_2 = p2.addRecombinant(g_2, g_1, breaks, NULL, NULL, NULL, "M");
        
        breaks = sim.chromosome.drawBreakpoints(individual);
        s_3 = p2.addRecombinant(g_1, g_2, breaks, NULL, NULL, NULL, "M");
        s_4 = p2.addRecombinant(g_2, g_1, breaks, NULL, NULL, NULL, "M");
      }
      else if (individual.sex == "F")
      {
        breaks = sim.chromosome.drawBreakpoints(individual);
        if (runif(1) <= 0.5)
          e = p2.addRecombinant(g_1, g_2, breaks, NULL, NULL, NULL, "F");
        else
          e = p2.addRecombinant(g_2, g_1, breaks, NULL, NULL, NULL, "F");
      }
    }
}
```

The definitions of `g_1` and `g_2` at the beginning are just shorthand, to keep the lines later in the callback from being so long that they wrap when shown here. As usual in nonWF models, this callback is called by SLiM once per individual in `p1`, giving the individual an opportunity to reproduce – in this model, an opportunity to produce gametes. The top-level loop causes the focal diploid individual to undergo meiosis exactly five times; this is an oversimplification, obviously, but there is no need, in most models, to generate millions of sperm. Within the loop, male individuals undergo meiosis by producing four sperm, whereas females produce just a single egg (plus three "polar bodies" that are discarded by meiosis in most sexual species, due to anisogamy; the polar bodies are not modeled here).

Gametes are produced by the `addRecombinant()` method, adding the resulting haploid individuals to `p2`. The calls to `addRecombinant()` here pass `NULL` for the genomes and breakpoints that generate the second genome of the offspring; this results in an empty second genome in the offspring, as is typical when modeling haploids in SLiM. The genomes used to generate the first genome of the offspring can be supplied as either (`g_1, g_2`) or (`g_2, g_1`); the first of the two genomes supplied is the copy strand at the beginning of recombination. Since the sperm generated use all of the genetic material from meiosis, both of those options are used (twice, because of the homologous chromosomes involved in meiosis); since egg generation produces only a single gamete, the choice of initial copy strand is randomized with a call to `runif()`.

Particularly for the sperm, since we want to generate the gametes in a realistic fashion following the rules of meiosis, we generate the recombination breakpoints ourselves and use them to generate complementary gametes. To generate breakpoints in the standard SLiM fashion, we call the `drawBreakpoints()` method of `Chromosome`; by default this produces a set of breakpoints identical to what SLiM would generate for its own internal use in reproduction. The number of recombination breakpoints generated is chosen by `drawBreakpoints()`, by default, using the overall recombination rate defined by the model.

Now let's look at the `reproduction()` callback for `p2`, which contains haploid gametes:

```
reproduction(p2, "F")
{
    mate = p2.sampleIndividuals(1, sex="M", tag=0);
    mate.tag = 1;
    
    child = p1.addRecombinant(individual.genome1, NULL, NULL,
      mate.genome1, NULL, NULL);
}
```

This callback is defined only for females – i.e., eggs. Each eggs gets to "reproduce" – be fertilized – to produce a new diploid organism in `p1`. In this model a random sperm is chosen to fertilize each egg, but one could easily implement phenomena such as sperm competition here to make the choice non-random. We mark sperm that have been used to fertilize an egg with a `tag` value of `1`, so that they will not be used again; when we draw a random sperm, we specify in the call to `sampleIndividuals()` that the sperm chosen must have a `tag` value of `0`, indicating that it has not already been used. Once the fertilizing sperm has been selected, it is tagged with a value of `1`, and the diploid zygote is generated with a call to `addRecombinant()`. The call to `addRecombinant()` here supplies only a single genome for each of the offspring genomes, with `NULL` for the breakpoint vectors; this makes the offspring's genomes a clonal copy of the corresponding genomes from the gametes. Normally, new mutations would be generated and added by SLiM during this clonal replication; we will fix that momentarily.

These callbacks implement the generation of gametes and then the fusion of gametes to produce diploid zygotes; but there is a little bit of additional machinery needed, which we implement in an `early()` callback that cleans up after reproduction and sets up for the next reproduction event:

```
early()
{
    if (sim.generation % 2 == 0)
    {
      p1.fitnessScaling = 0.0;
      p2.individuals.tag = 0;
      sim.chromosome.setMutationRate(0.0);
    }
    else
    {
      p2.fitnessScaling = 0.0;
      p1.fitnessScaling = K / p1.individualCount;
      sim.chromosome.setMutationRate(MU);
    }
}
```

In even-numbered generations the top half of this event will execute; in odd-numbered generations the bottom half will execute. In an even-numbered generation, at the point that early() events are called, p1 will have just generated gametes. This recipe assumes non-overlapping generations, so here we kill off the diploids by setting their `fitnessScaling` to `0.0`; `p1` will be emptied out completely. Next, we set the `tag` values of all of the gametes in `p2` to `0`; this marks all of the sperm as unused, in preparation for the way the `reproduction(p2)` callback uses the `tag` field. Finally, we set the mutation rate to `0.0`; we do not want new mutations to be generated by SLiM during fertilization, so we need to disable mutation temporarily.

In odd-numbered generations, gametes have just undergone fertilization, filling `p1` up with new diploid offspring. We therefore kill off the haploid gametes by setting their `fitnessScaling` to `0.0`; `p2` will be emptied out completely. Since each egg produces a zygote, we will have way too many diploids; we will be far above carrying capacity. The next line thus implements density-dependent selection on `p1`, as usual in nonWF models; note that no such density-dependence was imposed upon the gametes in this model. Finally, we set the mutation rate back up to the defined constant `MU`, since we want new mutations to arise during gamete production.

With this design, the population will flip back and forth between `p1` and `p2` and it flips between diploidy and haploidy, and the mutation rate will flip on and off as well. It would be straightforward to implement overlapping generations of diploids in this model; one could even delve into more esoteric ideas such as sperm storage. Fitness effects could differ in the haploid and diploid phases easily, by implementing `fitness()` callbacks that apply only to `p1` or `p2` as needed.

All that is left to finish off the model is a termination event, which here is trivial:

```
1000 late()
{
    sim.simulationFinished();
}
```

This approach to modeling the alternation of generations may be overkill in many practical situations. This model runs much more slowly than the equivalent model of only the diploid phase; for one thing, it is generating a population of gametes that is more than ten times larger than the population of diploids, every generation. Other strategies for modeling life cycle complexity may be usable instead; section 15.8, for example, presents a model of pollen flow between subpopulations of plants, which is simple to model without getting down to the details of modeling individual pollen grains and the sperm cells they produce as separate entities. Additional biological realism should generally be incorporated into a model only when there is reason to believe that it matters – that it would affect the results of the model. In some cases, however – such as when one wishes to have selection operate in the haploid phase – the additional biological realism of modeling alternation of generations may be useful.

Even more esoterically, one could use the same basic concepts to develop models of mating systems such as haplodiploidy; all that is really needed is to set up rules of reproduction that move the genomes around from individual to individual in the correct way using `addRecombinant()`, which is designed to be as flexible as possible in order to accommodate these sorts of purposes. Partitioning the population according to genetics – here, diploids versus haploids – is a trick that would probably also be useful in a model of haplodiploidy or other mating systems; indeed, such artificial partitioning can be very useful in other contexts too, such as storing non-reproducing juveniles separately from reproductive adults.

16. Tree-sequence recording: tracking population history and true local ancestry

This manual has already discussed a variety of ways of tracking ancestry in SLiM models, such as pedigree recording (section 13.2; see also section 15.12 for a related model) and using mutations to mark the population of origin of chromosome positions (section 13.9). In this chapter we will look at a very powerful way of tracking ancestry called tree-sequence recording. Tree-sequence recording is a new feature added in SLiM 3, and is introduced in some detail in section 1.7; you should read that section now if you haven't already. This is an advanced feature, and so this chapter will assume a familiarity with general SLiM and Eidos topics and techniques.

The use of tree-sequence recording leans heavily upon Python, where the tree sequence saved in a `.trees` file can be read, analyzed, and modified. To run most of the recipes in this chapter, you will need to have Python installed (Python 3.4.8 was used to construct and test these recipes). Some familiarity with Python will come in useful, but the Python scripts here will not be extensive. You will also need to have two Python packages installed: `msprime` and `pyslim`. The recipes in this chapter are based upon a minimum version of SLiM 3.1, `msprime` 0.6.1, and `pyslim` 0.1.

The `msprime` package is used to analyze tree sequences, overlay mutations onto a tree sequence, and perform coalescent simulations, among other tasks. The `msprime` project lives at https://github.com/tskit-dev/msprime, and installation instructions and documentation are there.

The `pyslim` package essentially provides a bridge between SLiM and `msprime`; it should be used to load SLiM `.trees` files into Python, to parse the SLiM-specific annotations in such files, to add such annotations to an existing tree sequence, and to write out SLiM-compliant `.trees` files. The `pyslim` project lives at https://github.com/tskit-dev/pyslim, and again, installation instructions and a link to its documentation are provided there.

In general, tree-sequence recording is compatible with all other SLiM features. It can be used with both WF and nonWF models, with all types of callbacks, with any population structure, and so forth. In this chapter we will not attempt to show a tree-seq version of every recipe we've already seen; instead we will focus upon the usage of the tree-sequence recording feature itself, to show what it is capable of and how it should be used. The early recipes will use `pyslim` only incidentally, to load `.trees` for use with `msprime`; later recipes will use `pyslim` more extensively.

16.1 A minimal tree-seq model

To begin, we will look at a minimal tree-sequence recording model based upon a simple neutral model. This recipe enables tree-seq recording and then runs much as usual:

```
initialize() {
    initializeTreeSeq();
    initializeMutationRate(0);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 1e8-1);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
}
5000 late() {
    sim.treeSeqOutput("./recipe_16.1.trees");
}
```

There are three notable differences here from the vanilla neutral model we have seen before. First, we now call `initializeTreeSeq()` to turn tree-seq recording on. This is all that is needed;

SLiM will now record all tree-sequence information throughout the run, and will automatically conduct simplification periodically using the default simplification interval (which can be customized with the `simplificationRatio` parameter to `initializeTreeSeq()`; see section 21.1).

Second, we now set the mutation rate to zero, because we don't want to model neutral mutations. Typically, when using tree-seq recording, neutral mutations are overlaid onto the ancestry tree after forward simulation has completed; we will show that technique in the next subsection, so in anticipation of that we have turned off neutral mutations here. Note that it is not *necessary* to turn off neutral mutations; there is no problem with including them in a tree-seq model, apart from the additional performance penalty of simulating them. It is just usually not desirable, because avoiding the overhead of simulating neutral mutations is one of the primary motivations for using tree-seq recording in the first place. Also, note that if the model had a mix of neutral and non-neutral mutations we would probably want to remove only the neutral mutations from the model, with a concomitant adjustment to the mutation rate; we will see an example of this in 16.3. (We would not want to remove the non-neutral mutations, since they affect the model's dynamics and thus cannot be overlaid after simulation.)

Third, we call `treeSeqOutput()` to write out a `.trees` file containing the full tree sequence that was recorded. This file is in a binary format defined by the `msprime` package (see section 23.4 for some details). However, it can be loaded back into SLiM with `readFromPopulationFile()`, just like a regular SLiM output file, and it can also be read in Python using `msprime`; we will see examples of both techniques in later recipes.

That's all there is to it; we will use the `.trees` file generated here in the next recipe, but for now we're done. It's worth noting, though, that an informal test of this model indicates that it runs in about 5 seconds, whereas the same model with tree-sequence recording turned off and a mutation rate of `1e-7` took 294 seconds to run. This performance improvement is not atypical; this is one major reason why tree-sequence recording is useful.

16.2 Overlaying neutral mutations

This recipe is actually a Python recipe, not a SLiM recipe. It depends upon having run the previous recipe, in section 16.1, to generate a `.trees` file representing the execution of a simple neutral model. Since mutation was turned off in that model, the `.trees` file contains no mutations; but it contains all of the ancestry information needed to overlay them. That is trivial in Python:

```
import msprime, pyslim

ts = pyslim.load("./recipe_16.1.trees").simplify()
mutated = msprime.mutate(ts, rate=1e-7, random_seed=1, keep=True)
mutated.dump("./recipe_16.1_overlaid.trees")
```

First we import the `msprime` and `pyslim` packages (which need to be installed, as discussed at the beginning of the chapter). Then we load the saved `.trees` file into a tree sequence object with `pyslim.load()`; this method, rather than `msprime.load()`, should generally be used to load SLiM `.trees` files since it knows how to handle SLiM metadata and SLiM provenance information.

We then call `simplify()` to simplify the loaded tree sequence. SLiM 3.1 produces `.trees` files that contain the first ancestral individuals in each new subpopulation created by `addSubpop()`; these individuals are useful for various purposes, such as recapitation (see section 16.10) and tracing ancestry, so they are provided by SLiM for convenience. However, they are not marked as "remembered", so they disappear when the tree sequence is simplified; this makes it easy to get rid of them when they are not wanted. Here we do not need them (although they would do no harm), so we simplify them away to demonstrate this typical usage pattern. Note that this means that mutations will be overlaid only back to the point of coalescence; if we want fixed mutations overlaid past coalescence back to the start of forward simulation, we should not `simplify()`.

Next, we overlay mutations with `msprime.mutate()` to generate a new tree sequence (with a given mutation rate and random number generator seed), and finally we write the mutated tree sequence out to a new `.trees` file. The `keep=True` parameter to `msprime.mutate()` indicates that any existing mutations should be kept, not overwritten; in this example there are no mutations already present in the tree, but if there were, we would typically want to keep them.

This script runs in about `0.2` seconds. Why is it so much faster than modeling the neutral mutations in SLiM? The key is that when mutations are overlaid after the forward simulation has completed, they only need to be generated along those branches of the ancestry tree that led to extant individuals at the end of the run. All of the branches of the evolutionary tree that went extinct – the vast majority of branches, in most models – need not have mutations overlaid.

The new `.trees` file written out at the end could be read by a different Python script to perform further analysis or modification, again using `msprime` and `pyslim`. We could also, instead, simply work with the new tree sequence object in further analysis code in this script; or we could write out the mutation information to a different file format, such as MS format, if the ancestry information encapsulated by the `.trees` file is no longer needed.

It should also be possible to read a `.trees` file with overlaid mutations back into SLiM with the `readFromPopulationFile()` method, to use its state as the starting point for further forward simulation. However, to do that the mutation information provided by `msprime` would need to be annotated with additional data required by SLiM about the overlaid mutations, such as their selection coefficients and mutation types. Furthermore, mutation positions would have to be rounded, or somehow guaranteed to be integers already, since SLiM expects integer mutation positions. We will add a recipe showing these techniques when it becomes possible.

16.3 Simulation conditional upon fixation of a sweep, preserving ancestry

In the recipe of section 16.1 we saw a tree-seq model for a trivial neutral model, but this method is not limited to neutral models. Here we will look at a model involving both neutral and deleterious mutations, into which a beneficial mutation is introduced. We want the beneficial mutation to sweep, and we want this model to run conditional upon a successful sweep. This will be quite similar to the recipe of section 10.2, then; however, here we have a background of deleterious as well as neutral mutations. When we convert the model to use tree-sequence recording, we will remove the neutral mutations from the model (since they can be overlaid later, as in section 16.2). The ancestry information for all of the individuals in the model will be preserved, even though the model will restart itself repeatedly until fixation is achieved.

First, here is the model without tree-sequence recording:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "g", -0.01, 1.0);  // deleterious
    initializeMutationType("m3", 1.0, "f", 0.05);        // introduced
    initializeGenomicElementType("g1", c(m1, m2), c(0.9, 0.1));
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    defineConstant("simID", getSeed());
    sim.addSubpop("p1", 500);
}
```

```
1000 late() {
    target = sample(p1.genomes, 1);
    target.addNewDrawnMutation(m3, 10000);
    sim.outputFull("/tmp/slim_" + simID + ".txt");
}
1000:100000 late() {
    if (sim.countOfMutationsOfType(m3) == 0) {
       if (sum(sim.substitutions.mutationType == m3) == 1) {
          cat(simID + ": FIXED\n");
          sim.simulationFinished();
       } else {
          cat(simID + ": LOST - RESTARTING\n");

          sim.readFromPopulationFile("/tmp/slim_" + simID + ".txt");
          setSeed(rdunif(1, 0, asInteger(2^32) - 1));
       }
    }
}
```

Since this is very similar to the recipe of section 10.2, we won't discuss it here; see that section for discussion. Here, our goal is to convert it into a tree-seq model:

```
initialize() {
    initializeTreeSeq();
    initializeMutationRate(1e-8);
    initializeMutationType("m2", 0.5, "g", -0.01, 1.0);  // deleterious
    initializeMutationType("m3", 1.0, "f", 0.05);        // introduced
    initializeGenomicElementType("g1", m2, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 {
    defineConstant("simID", getSeed());
    sim.addSubpop("p1", 500);
}
1000 late() {
    target = sample(p1.genomes, 1);
    target.addNewDrawnMutation(m3, 10000);
    sim.treeSeqOutput("/tmp/slim_" + simID + ".trees");
}
1000:100000 late() {
    if (sim.countOfMutationsOfType(m3) == 0) {
       if (sum(sim.substitutions.mutationType == m3) == 1) {
          cat(simID + ": FIXED\n");
          sim.treeSeqOutput("slim_" + simID + "_FIXED.trees");
          sim.simulationFinished();
       } else {
          cat(simID + ": LOST - RESTARTING\n");

          sim.readFromPopulationFile("/tmp/slim_" + simID + ".trees");
          setSeed(rdunif(1, 0, asInteger(2^32) - 1));
       }
    }
}
```

We have added a call to `initializeTreeSeq()`, and changed the file save and load code to use a `.trees` file instead of a standard SLiM text output file. We also removed the neutral mutations from the model; note that this required changing the mutation rate. Since 90% of the mutations in the original model were neutral, the new model has a mutation rate one-tenth as high, so that the rate of deleterious mutations remains unchanged. In this simple model, with only one genomic element type, the adjustment to the mutation rate is very straightforward; in a model with a more complex genetic architecture in which the fraction of mutations that are neutral varies from region to region along the chromosome, the necessary adjustment to the mutation rate after removal of neutral mutations might require switching to a mutation-rate map, rather than using a single fixed mutation rate. A mutation-rate map may be supplied to `initializeMutationRate()`, rather than a single fixed rate; see section 21.1.

Otherwise, the model is unchanged. This model will run in much the same manner as the first version, restarting itself whenever the `m3` mutation is lost until it achieves fixation. The deleterious mutations present when the beneficial mutation is introduced will be saved to the `.trees` file and restored each time the model restarts.

When this model achieves fixation, it writes out the final state of the model to a new `.trees` file (not in the `/tmp` directory, this time). This file can be loaded into Python with `pyslim`, as in the recipe of section 16.2, to overlay neutral mutations, or to perform any other analysis desired. Note that since this model contains non-neutral mutations as well as neutral mutations, the mutation rate used in neutral mutation overlay would not be the original rate of `1e-7`, but instead the rate specifically of *neutral* mutations along the chromosome, and that with a complex genetic architecture this might necessitate the specification of a mutation-rate map rather than the use of a single fixed rate, similarly to the issue with the mutation rate in SLiM discussed above.

16.4 Detecting the "dip in diversity": analyzing tree heights in Python

It has been mentioned several times that one can perform "other analysis" in Python using the information saved in a `.trees` file. In this recipe and the next, we will look at two examples. Because `.trees` files contain information about the true local ancestry of every location along the genome of every extant individual, including the times when recombination and mutation events occurred in the past, there are many interesting analyses that can be conducted.

The recipe in this section will model "background selection", which is the effect of selection against deleterious mutations upon nearby neutral sites. Background selection is, in a sense, similar to "genetic hitchhiking", which is the effect of selection for beneficial mutations upon nearby neutral sites. Although they are different, both of these types of so-called "linked selection" have been found to reduce genetic diversity in non-coding regions near genes; because mutations within genes often have functional effects (whether positive or negative), they often exert linked selection upon nearby neutral regions that reduces diversity. The reduction in diversity falls off as distance to the nearest gene increases, producing a characteristic "dip in diversity" near genes (Charlesworth et al. 1993; Hudson 1994; Sattath et al. 2011; Elyashiv et al. 2016).

The SLiM model for this is complicated only because, for higher statistical power, we want to model many genes interspersed with many non-coding regions, so that a single run of the model generates enough data for us to see the effect we're interested in:

```
initialize() {
    defineConstant("N", 10000);  // pop size
    defineConstant("L", 1e8);    // total chromosome length
    defineConstant("L0", 200e3); // between genes
    defineConstant("L1", 1e3);   // gene length
    initializeTreeSeq();
    initializeMutationRate(1e-7);
    initializeRecombinationRate(1e-8, L-1);
    initializeMutationType("m2", 0.5, "g", -(5/N), 1.0);
    initializeGenomicElementType("g2", m2, 1.0);
```

```
        for (start in seq(from=L0, to=L-(L0+L1), by=(L0+L1)))
            initializeGenomicElement(g2, start, (start+L1)-1);
    }
    1 {
        sim.addSubpop("p1", N);
        sim.rescheduleScriptBlock(s1, 10*N, 10*N);
    }
    s1 10 late() {
        sim.treeSeqOutput("./recipe_16.4.trees");
    }
```

The chromosome is defined as a set of genes of length `L1`, separated by non-coding regions of length `L0`. The model doesn't define the non-coding regions with genomic elements; we don't want mutations to occur in the non-coding regions, since we will not need any neutral mutations to conduct our analysis (and even if we did, it would be better to overlay them afterwards in Python). A subpopulation of size *N* is defined, and then the final output event is rescheduled to generation 10*N* (a rough guess at a coalescence time for the model; the results will not be terribly sensitive to the accuracy of this guess since diversity near the genes will be suppressed continuously throughout the run of the model).

To run this model and then conduct the analysis, we can run the following Python script (assuming that we're in the directory containing the SLiM model file):

```
import subprocess, msprime, pyslim
import matplotlib.pyplot as plt
import numpy as np

# Run the SLiM model and load the resulting .trees
subprocess.check_output(["slim", "-m", "-s", "0", "./recipe_16.4.slim"])
ts = pyslim.load("./recipe_16.4.trees").simplify()

# Measure the tree height at each base position
height_for_pos = np.zeros(int(ts.sequence_length))
for tree in ts.trees():
    mean_height = np.mean([tree.time(root) for root in tree.roots])
    left, right = map(int, tree.interval)
    height_for_pos[left: right] = mean_height

# Convert heights along chromosome into heights at distances from gene
height_for_pos = height_for_pos - np.min(height_for_pos)
L, L0, L1 = int(1e8), int(200e3), int(1e3)
gene_starts = np.arange(L0, L - (L0 + L1) + 1, L0 + L1)
gene_ends = gene_starts + L1 - 1
max_d = L0 // 4
height_for_left = np.zeros(max_d)
height_for_right = np.zeros(max_d)
for d in range(max_d):
    height_for_left[d] = np.mean(height_for_pos[gene_starts - d - 1])
    height_for_right[d] = np.mean(height_for_pos[gene_ends + d + 1])
height_for_distance = np.hstack([height_for_left[::-1], height_for_right])
distances = np.hstack([np.arange(-max_d, 0), np.arange(1, max_d + 1)])

# Make a simple plot
plt.plot(distances, height_for_distance)
plt.show()
```

After importing packages, we run the SLiM model with `subprocess.check_output()`, which generates the `recipe_16.4.trees file`. We read that file in using `pyslim.load()` and gather tree heights, which are a proxy for diversity, from it; but let's examine that process step by step.

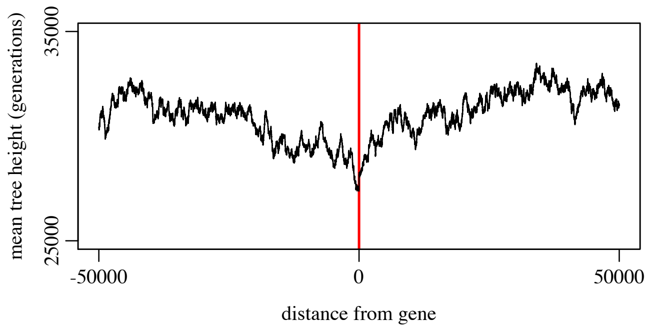
First of all, `pyslim.load()` reads in the `.trees` file as tree sequence, which is a collection of ancestry trees (section 1.7 introduces these concepts, but we will quickly review them here). The tree sequence thinks of the genome as being divided into successive intervals, each of which has a particular pattern of ancestry. Because the ancestry at adjacent positions along the genome tends to be highly correlated, this representation makes the tree sequence very compact and efficient. When we loop over the trees in `ts.trees`, we are actually looping over these chromosome intervals, getting the ancestry tree for each successive interval.

Second, the ancestry tree for a given interval is not quite a tree in the usual sense, because it can have multiple roots. This is because a given position will not necessarily share a common ancestor, in forward simulation; at the beginning of simulation every individual is an island unto itself, with no known relationship to any other individual, and ancestral relationships will be constructed by coalescence as the model runs forward. The tree for a given interval, in a simulation of *N* individuals, might therefore have anywhere from one root (if coalescence has produced a single common ancestor for the whole population) to *N* roots (if no coalescence has occurred yet). When we loop over roots in `tree.roots`, we are looping over common ancestors shared by subsets of the extant population.

The code gathers tree heights across all roots for the current interval, using `tree.time(root)`, and uses `np.mean()` to get the mean height. This is our metric of diversity for the interval. Since an interval can span more than one base position, we replicate that mean height across the tree's interval in `height_for_pos`, which we want to have a height value for each base position.

Note that in this recipe the `simplify()` of the loaded tree sequence is essential (whereas in section 16.2 it was not); without it, every tree would have a root in the first generation, in one or another original ancestor, and all the tree heights would be the same. The `simplify()` strips away the original ancestors, giving us trees with roots representing the most recent common ancestors for each tree.

With that done, we now need to convert that vector of tree heights along the chromosome into heights at a given distance from the nearest gene. This involves a sort of descrambling of the data based upon the genetic structure of the model, which (as described above) interleaved non-coding regions of length `L0` with genes of length `L1`. The details of this descrambling aren't worth getting into in detail; this is just data analysis, and is fairly routine Python code with no dependency upon `msprime` or SLiM. The end result of this analysis is a vector named `height_for_distance` that has mean heights for the corresponding distances in the vector `distances`. This is what we wanted, so we can plot it (this plot is prettified using R code not shown here, but the Python plot looks essentially the same):



This plot is noisy; that could presumably be smoothed out with more genes on a longer chromosome, a larger population size, and averaging across multiple runs of the model. Nevertheless, the "dip in diversity" is very clear: the mean tree height drops to a clear minimum value precisely at zero on the plot.

Note that this analysis is not based upon the patterns of neutral mutation diversity around the simulated genes. Instead, the pattern of inheritance itself – the mean time to the most recent common ancestor at each base position – is used to generate the plot. This is far more powerful than using the pattern of neutral mutation diversity, because neutral mutations are sparse and stochastic. You certainly could overlay neutral mutations onto the tree sequence, as we did in section 16.2, and then feed that into the analysis methods used by empirical studies (and perhaps that would be a useful thing to do, to test the power or accuracy of those empirical methods). But the analysis here is, in a sense, the average across many such analyses – across an infinite number of such mutation overlays, in fact – and so it is far more powerful.

This recipe shows an analysis using just one metric provided by `msprime`, the height of a given root using `tree.time(root)`. The ancestry information provided by the tree sequence could be mined in countless other ways. In the next recipe, we will look at another example of post-simulation analysis using `msprime`.

16.5 Mapping admixture: analyzing ancestry in Python

It is often useful to be able to trace the true local ancestry at each location along the chromosome. In section 13.9, a recipe was presented that provided this ability by introducing a marker mutation at every base position along the chromosome in all of the individuals of one subpopulation, while leaving the other subpopulation unmarked. After admixture of the two subpopulations, the ancestry of each individual at each position could be determined by the presence or absence of the marker mutation. That method works, but it comes at a cost of considerable overhead in both runtime and memory usage. A chromosome of length `1e6` is close to the practical limit for that recipe; a chromosome of length `1e8` is estimated by extrapolation to take 7.2 days to run and – even worse – to require 8.1 TB of memory. Since the tree sequence is a sparse data structure that records information about the ancestry at each chromosome position in a highly compact form, one might suppose that it could provide information about true local ancestry more efficiently, and indeed it can.

In this section we will look at a recipe very similar to that of section 13.9; refer back to that section for further discussion of the design and motivation of that model. Here we will not use marker mutations; instead we will use tree-sequence recording:

```
initialize() {
    defineConstant("L", 1e8);
    initializeTreeSeq();
    initializeMutationRate(0);
    initializeMutationType("m1", 0.5, "f", 0.1);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, L-1);
    initializeRecombinationRate(1e-8);
}
1 late() {
    sim.addSubpop("p1", 500);
    sim.addSubpop("p2", 500);
    sim.treeSeqRememberIndividuals(sim.subpopulations.individuals);

    p1.genomes.addNewDrawnMutation(m1, asInteger(L * 0.2));
    p2.genomes.addNewDrawnMutation(m1, asInteger(L * 0.8));
```

```
        sim.addSubpop("p3", 1000);
        p3.setMigrationRates(c(p1, p2), c(0.5, 0.5));
    }
    2 late() {
        p3.setMigrationRates(c(p1, p2), c(0.0, 0.0));
        p1.setSubpopulationSize(0);
        p2.setSubpopulationSize(0);
    }
    2: late() {
        if (sim.mutationsOfType(m1).size() == 0)
        {
           sim.treeSeqOutput("./recipe_16.5.trees");
           sim.simulationFinished();
        }
    }
    10000 late() {
        stop("Did not reach fixation of beneficial alleles.");
    }
```

Only two mutations ever exist in this model: the beneficial mutations introduced at 0.2*L* in `p1` and at 0.8*L* in `p2`. After admixture to form `p3`, when both mutations have fixed, a `.trees` file is written out and the simulation ends. The `.trees` file will then be read and analyzed in Python, as we will see below.

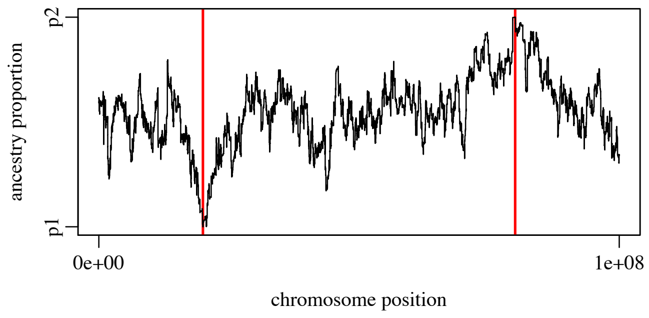
The only twist here is the call to `sim.treeSeqRememberIndividuals()`. Our goal is to trace the ancestry at each position in each individual to either `p1` or `p2`. In point of fact, in SLiM 3.1 and later this call is not strictly necessary, because the original ancestors of each subpopulation created by `addSubpop()` are kept by SLiM automatically. If we did not `simplify()` after loading the tree sequence with pyslim, those ancestors would be available for us to trace ancestry back to, allowing us to determine whether a particular genomic region originated in `p1` or `p2`. We have shown the call here, however, for a couple of reasons: (1) it makes the way this recipe works more explicit and less magic, (2) you may wish to remember other individuals in a simulation to trace ancestry back to them, so showing the `treeSeqRememberIndividuals()` call here makes it clear how to do that, and (3) by explicitly remembering the ancestors we can `simplify()` on load, which may be desirable – we may want to have a simplified tree sequence for other purposes.

The run of the SLiM model, along with post-run analysis and plotting, is all done in a single Python script, as before:

```
    import subprocess, msprime, pyslim
    import matplotlib.pyplot as plt
    import numpy as np

    # Run the SLiM model and load the resulting .trees file
    subprocess.check_output(["slim", "-m", "-s", "0", "./recipe_16.5.slim"])
    ts = pyslim.load("./recipe_16.5.trees").simplify()

    # Load the .trees file and assess true local ancestry
    breaks = np.zeros(ts.num_trees + 1)
    ancestry = np.zeros(ts.num_trees + 1)
    for tree in ts.trees(sample_counts=True):
        subpop_sum, subpop_weights = 0, 0
        for root in tree.roots:
            leaves_count = tree.num_samples(root) - 1  // the root is a sample
            subpop_sum += tree.population(root) * leaves_count
            subpop_weights += leaves_count
        breaks[tree.index] = tree.interval[0]
        ancestry[tree.index] = subpop_sum / subpop_weights
    breaks[-1] = ts.sequence_length
    ancestry[-1] = ancestry[-2]

    # Make a simple plot
    plt.plot(breaks, ancestry)
    plt.show()
```

After imports, the SLiM model (named `recipe_16.5.slim`) is run with subprocess, and the `.trees` file saved by the model is then read in using `pyslim.load()` as usual, with a `simplify()` call since we have explicitly remembered the ancestors we are interested in (see discussion above). We then loop over the trees in the tree sequence, and over the roots for each tree (see section 16.4 for discussion of these concepts). For each root, we want to assess ancestry as tracing back to either `p1` or `p2`; this can be done simply by calling `tree.population(root)`, since every node in the tree sequence is marked with its subpopulation of origin. We average the ancestry of all roots for an interval to get the mean ancestry, but this is a weighted average; each root is weighted according to the number of descendants it has, effectively computing the average ancestry across all extant individuals, rather than across roots. The start position on the chromosome is recorded in parallel with these calculated mean ancestry values, and a terminating entry in both vectors brings us to the end of the chromosome.

That's it for the analysis; this model is much simpler structurally than the previous recipe. All that is left is to plot the data. The values in `starts` and `ends` are used as the endpoints of line segments, interleaved with `zip()`; the mean ancestries in `subpops` are duplicated to match. (For those not familiar with Python, these lines may seem a bit magical, sorry.) The final plot (produced by an R script for polish, rather than by the Python code here) looks like:



This is much the same as what the recipe of section 13.9 provided. Since the two beneficial mutations both fixed, the ancestry of the final population is pure, `p1` or `p2`, at the points where they were introduced. The ancestry then shades continuously (but stochastically) between those two points due to recombination (see section 13.9 for further discussion). The SLiM model here took only 0.415 seconds to run, however – somewhat of an improvement over 7.2 days. The post-run analysis took about 62 seconds; looping over all of the roots of all of the trees in the tree sequence is not entirely trivial, but is still far simpler than simulating `1e8` marker mutations in SLiM.

This recipe will generalize easily to any number of ancestral subpopulations, as long as the original founders of each subpopulation are remembered with `treeSeqRememberIndividuals()` so that ancestry can be traced back to them (of course taking the mean of the subpopulations of the tree roots wouldn't be the right analysis then). Since every node knows the subpopulation to which it belonged, the ancestral history at each position can be assessed by walking up the ancestry chain from the extant nodes to the roots, as long as one ensures that the appropriate ancestors are remembered forever; one might remember every individual that migrates to a new subpopulation, for example, using the `migrant` property of `Individual`, so that the migratory history through the ancestry tree can be traced. All of this goes far beyond what would be reasonable to implement with marker mutations using the methods of section 13.9.

16.6 Measuring the coalescence time of a model

A common problem in forward simulation is deciding how to conduct model burn-in. A burn-in period is a period of simulation executed in order to arrive at an appropriate starting state for the model one wishes to execute; often this starting state is for a neutral model at equilibrium, but not necessarily so. But how long should the burn-in period be, to provide such an equilibrium state? Running until coalescence ensures that no genetic diversity in the population could date back to the start of the simulation, so all polymorphic loci derive from after the start of the simulation. However, to attain equilibrium takes longer: in a truly neutral population of constant size, a total of two or three times the time required to reach coalescence should suffice. But that just kicks the can down the road; how long does it take to achieve coalescence? A heuristic of 10*N* is often used: run for ten times the population size (*N*), in generations. But this heuristic is less than satisfactory; the model may not have coalesced even at 10*N* generations, or it may have coalesced long before (meaning wasted simulation time). And with any additional complexity, such as multiple subpopulations connected by migration, the 10*N* rule is potentially even more problematic. What to do?

Tree-sequence recording provides a very easy solution, because the ancestry information that it records is well-suited to determining whether the model has achieved coalescence. The only complication is that coalescence can only be evaluated immediately after simplification has been performed; the coalescence test requires that the tree sequence be in a simplified state. SLiM largely hides this detail from the user; you can query the coalescence state at any time, but the answer you get will actually be the coalescence state at the time that the last simplification was performed, not the state at the present time. Sometimes, then, one will want to exert some control over the simplification process, so that one knows at what granularity coalescence is actually being assessed, as described below.

Here is a recipe demonstrating the coalescence-detection technique:

```
initialize() {
    initializeTreeSeq(checkCoalescence=T);
    initializeMutationRate(0);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 1e8-1);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
}
1: late() {
    if (sim.treeSeqCoalesced())
    {
       catn(sim.generation + ": COALESCED");
       sim.simulationFinished();
    }
}
100000 late() {
    catn("NO COALESCENCE BY GENERATION 100000");
}
```

This model turns on coalescence checking with `checkCoalescence=T` (see section 21.1; coalescence checking needs to be turned on explicitly because there is a small performance penalty associated with it). Then, every generation, we check for coalescence with `sim.treeSeqCoalesced()`. As mentioned above, this only tells us whether coalescence was observed at the last simplification; when auto-simplification finds that coalescence has occurred, `treeSeqCoalesced()` will then return `T` when it is next called. Usually it is not necessary to detect coalescence in the very generation in which it occurs; it is typically enough to simply know that it has occurred at some recent time, as this model does.

When this model is run, typical output looks like this:

```
9984: COALESCED
```

Coalescence was probably achieved some time before generation `9984`; `9984` is just the generation in which auto-simplification *noticed* that coalescence. Note that this is higher than the 10*N* value of `5000` (and auto-simplification occurs every couple of hundred generations in this model); so at generation `5000` the model would not yet have coalesced. The time to coalescence is variable, depending as it does upon stochastic events, but repeated runs of this model will show that in fact it typically coalesces around `10000` generations, or approximately 20*N*.

To control the granularity of coalescence checking more precisely, one may turn off auto-simplification by passing `simplificationRatio=INF` to `initializeTreeSeq()`, and then call `treeSeqSimplify()` to simplify on demand, after which `treeSeqCoalesced()` will return an up-to-date assessment. Simplifying every generation is very slow, however, so simplifying and checking at a regular interval, such as every hundredth generation, is generally preferable.

Note that certain actions in script, such as adding a new subpopulation, can break the coalescence of a model; all of the individuals in the population no longer share a common ancestor, even though they previously did. The value returned by `treeSeqCoalesced()` will not immediately reflect this; instead, as usual, that value will reflect the coalescence state after the last simplification that was performed. If this poses a problem, one can always explicitly simplify immediately after such model events, forcing the coalescence state to be re-checked.

Coalescence checking will work in all types of models (with the above caveats about timing and granularity), regardless of selection, population structure, etc. However, coalescence is only a useful indicator of the timescale needed for equilibration in fairly simple neutral models. If model dynamics during burn-in change over time, or are substantially non-neutral, coalescence may be a poor indicator of equilibration; indeed, such models may not even have an equilibrium state. What constitutes a proper burn-in for such models is a difficult question.

It is worth noting that the point of coalescence, in a forward simulation, is not itself an unbiased or equilibrium state. In particular, as a forward simulation runs the mean tree height will grow over time until coalescence is reached, at which point it will drop suddenly (because a more recent common ancestor has just emerged); then it will rise steadily again until the next coalescence, at which point it will again drop, and so forth. A plot of mean tree height over time therefore exhibits a "saw-tooth" pattern, and the moment of any given coalescence event is the bottom point of one saw-tooth – a special point in time, not a typical or average one. It is therefore advisable to continue neutral burn-in well beyond the point of coalescence; this is why, at the beginning of this subsection, we recommended running for two or three times the time required to reach coalescence. For an even better solution to this problem of neutral burn-in, see the "recapitation" technique described in section 16.10.

16.7 Analyzing selection coefficients in Python with `pyslim`

So far we have used the `pyslim` package only minimally, to load in `.trees` files generated by SLiM. The next several recipes will delve into its capabilities more. In this section, we will see how to use `pyslim` to obtain SLiM-specific information about a simulation from the metadata stored in the `.trees` file generated by SLiM.

Let's begin with a simple SLiM model of beneficial and neutral mutations on a uniform chromosome:

```
initialize() {
    initializeTreeSeq();
    initializeMutationRate(1e-10);
    initializeMutationType("m1", 0.5, "g", 0.1, 0.1);
    initializeMutationType("m2", 0.5, "g", -0.1, 0.1);
    initializeGenomicElementType("g1", c(m1, m2), c(1.0, 1.0));
    initializeGenomicElement(g1, 0, 1e8-1);
    initializeRecombinationRate(1e-8);
}
1 {
    sim.addSubpop("p1", 500);
}
20000 late() { sim.treeSeqOutput("./recipe_16.7.trees"); }
```

Beneficial mutations are drawn from a gamma DFE with a mean of `0.1`, deleterious mutations from a gamma DFE with a mean of `-0.1`. After the model has run for a while, the expectation would be that the mutations generated as the model runs would indeed have those means, but that the mutations fixed would be biased towards the higher end of the distribution for both mutation types. This would be simple enough to evaluate in Eidos at the end of the model run, but let's do it in Python instead, using `pyslim`, as a proof on concept. Here is a Python script that assumes that a `.trees` file has been saved to the path used by the model above (we've shown already how to run a SLiM model from inside Python using `subprocess.check_output()`, so there's no need to keep reiterating that point):

```
import msprime, pyslim

ts = pyslim.load("recipe_16.7.trees").simplify()

coeffs = []
for mut in ts.mutations():
    md = pyslim.decode_mutation(mut.metadata)
    sel = [x.selection_coeff for x in md]
    if any([s != 0 for s in sel]):
        coeffs += sel

b = [x for x in coeffs if x > 0]
d = [x for x in coeffs if x < 0]

print("Beneficial: " + str(len(b)) + ", mean " + str(sum(b) / len(b)))
print("Deleterious: " + str(len(d)) + ", mean " + str(sum(d) / len(d)))
```

We start by loading the `.trees` file with `pyslim.load()` as usual. We then loop through all of the mutations in the tree sequence, provided by `ts.mutations()`. We are interested in the selection coefficients of the mutations, which are not part of the base information provided by the `.trees` format; instead, they are stored in SLiM-specific metadata attached to each mutation. To access them, then, we ask pyslim to decode the metadata for us, from the binary format it is in, and return it to us, using the `pyslim.decode_mutation()` method. We can then fetch selection coefficients (more on this in a moment) and append them to the `coeffs` list. Once we have that list, it is a trivial matter to select the beneficial and deleterious mutations from it and print a summary of each. A test run produces this output:

```
Beneficial: 3580, mean 1.0382685732466397
Deleterious: 103, mean -0.04902286211917154
```

A great many more beneficial mutations than deleterious mutations are present, even though they arise at equal rates in the SLiM model, which is unsurprising. Furthermore, the mean of the mutations present is considerably biased relative to the mean of the DFEs for these mutation types (which were `0.1` and `-0.1`).

There are a few points to note here, regarding the way in which the selection coefficients are gathered. First of all, the tree sequence retains fixed mutations, unlike SLiM. As the SLiM model ran, mutations that fixed were converted to substitutions as usual in SLiM; but in the tree-sequence no such conversion occurs. The list of mutations provided by the tree sequence therefore includes both fixed and segregating mutations; no distinction is made.

Second, note that the return value from `pyslim.decode_mutation()` is a list, not a single object. We end up looping through the elements in this list and getting a selection coefficient from each element. The reason for this has to do with mutation stacking in SLiM (see section 1.5.3 for a review of this concept). A "mutation", as far as the tree sequence is concerned, is a unique *mutational state* at a given position, which encompasses all of the mutations that have stacked at that position. When we call `pyslim.decode_mutation()`, it helpfully deconstructs this stacked state into the component mutations within it. If a particular mutation occurs in more than one configuration in the tree sequence – by itself at a position and also stacked with another mutation at that position, in different genomes, say – we will actually encounter that mutation more than once during this process, and we will therefore overcount it. Since stacking will be extremely uncommon in this model, we don't worry about it much; it will not skew our results noticeably. If we wanted to be more rigorous, however, we could use the mutation IDs from SLiM (also available through `pyslim`) to construct a uniqued list of mutations, with each mutation counted only once even if it is stacked with other mutations in various ways, and could then do the rest of the analysis using that uniqued list. Since that is just elementary Python wrangling, we will not go into that level of detail here.

16.8 Starting a hermaphroditic WF model with a coalescent history

In section 16.6, we saw how to assess whether a model has coalesced or not using `treeSeqCoalesced()`, allowing us to run a model for an appropriate burn-in period rather than relying upon the (problematic) 10*N* heuristic. If the burn-in period for a model is neutral and can be run with `msprime`'s coalescent simulation, we can avoid running our burn-in with forward simulation at all. Instead, we can run the burn-in period using the coalescent, save the result as a `.trees` file (annotated with `pyslim` as needed), and load the result into SLiM where we continue the simulation from the endpoint of the coalescent. This may sound complicated, but in fact it is remarkably simple.

However, note that starting a simulation with the coalescent in this way is often not the best technique. In many cases, the "recapitation" technique presented in section 16.10 is superior, for reasons that will be explained there. This recipe is for primarily for illustration.

We begin with a Python script:

```
import msprime, pyslim

ts = msprime.simulate(sample_size=10000, Ne=5000, length=1e8,
    mutation_rate=0.0, recombination_rate=1e-8)
slim_ts = pyslim.annotate_defaults(ts, model_type="WF", slim_generation=1)
slim_ts.dump("recipe_16.8.trees")
```

The `msprime.simulate()` method is used to run a coalescent simulation with n=2N_e=`10000` (n being a haploid sample size, N_e being in terms of diploids), a chromosome of length `1e8`, and a recombination rate of `1e-8`. A mutation rate of `0.0` is used, since we only want the coalescent history, not mutations within it (those can be overlaid later if needed). This returns a tree sequence object, but it is in `msprime`'s format; it does not have any of the metadata annotations expected by SLiM. The next step is to use `pyslim.annotate_defaults()` to add those annotations. We tell it to annotate the data for a WF SLiM model, and to align the times in the tree sequence so that the current generation has index `1`; when we load the model into SLiM, it will start at generation `1` even though there are many generations of history stretching back in time. After annotating, the `.trees` file is saved.

Now we can run a SLiM model that loads it and continues the run with some non-neutral dynamics:

```
initialize() {
    initializeTreeSeq();
    initializeMutationRate(0);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "f", 0.1);
    initializeGenomicElementType("g1", m2, 1.0);
    initializeGenomicElement(g1, 0, 1e8-1);
    initializeRecombinationRate(1e-8);
}
1 late() {
    sim.readFromPopulationFile("recipe_16.8.trees");
    target = sample(sim.subpopulations.genomes, 1);
    target.addNewDrawnMutation(m2, 10000);
}
1: {
    if (sim.mutationsOfType(m2).size() == 0) {
       print(sim.substitutions.size() ? "FIXED" else "LOST");
       sim.treeSeqOutput("recipe_16.8_II.trees");
       sim.simulationFinished();
    }
}
2000 { sim.simulationFinished(); }
```

At the end of this model (note that an initial seed of `2178208680098` produces fixation in SLiM 3.1), a new `.trees` file is saved out. This contains the full ancestry information for the simulation – not just for the period simulated in SLiM, but also for the coalescent. Just to verify here that the full history is present, let's check the final tree sequence:

```
import msprime, pyslim

ts = pyslim.load("recipe_16.8_II.trees").simplify()

for tree in ts.trees():
    for root in tree.roots:
        print(tree.time(root))
```

This just prints the heights of the trees in the final tree sequence; in a test run, it prints a wide range of values, ranging from less than 10,000 to more than 60,000. The simulation is fully coalesced (that could be confirmed by checking that the number of roots per tree is always exactly

1), but it reached coalescence at different times at different positions along the chromosome, so the tree heights are not all identical. However, all of the heights are considerably larger than the 324 generations that the SLiM model ran for; the rest is the height of the coalescent history, which has indeed been preserved. We could now overlay neutral mutations upon the final .trees file as we did in section 16.2, or perform ancestry analyses with it such as those we did in section 16.4 and 16.5, or whatever else we might wish to do.

16.9 Starting a sexual nonWF model with a coalescent history

In the previous recipe, we saw how to run an msprime coalescent simulation as a burn-in period and save it as a SLiM-compliant .trees file which could then be used to run non-neutral dynamics on top of the coalescent burn-in history. The scenario presented there was very simple, however: a hermaphroditic WF model. What if we want to use msprime to construct a coalescent burn-in for a model complex model? We will need to annotate the tree sequence appropriately for the type of model that we intend to load it into in SLiM. Here we will see how to do this for a sexual nonWF model. As mentioned in the previous recipe, however, starting a simulation with the coalescent is often not the best technique; the "recapitation" technique presented in section 16.10 is usually preferable, for reasons discussed there. This recipe is offered for illustration of the relevant techniques.

To get SLiM to accept the .trees file from the burn-in as legitimate input for a sexual nonWF model, we will need to assign sexes to each individual. We will assign ages too; if we didn't do so, all of the individuals would be given a default age of 0, but here we would like the initial population to have some age structure. Finally, we will tell pyslim to mark the tree sequence as being from a nonWF simulation, so that it matches SLiM's expectations.

The Python script for this recipe is a bit longer, naturally, since the annotation adds a bit of complication:

```
import msprime, pyslim, random

ts = msprime.simulate(sample_size=10000, Ne=5000, length=1e8,
    mutation_rate=0.0, recombination_rate=1e-8)

tables = ts.dump_tables()
pyslim.annotate_defaults_tables(tables, model_type="nonWF",
    slim_generation=1)
individual_metadata = list(pyslim.extract_individual_metadata(tables))
for j in range(len(individual_metadata)):
    individual_metadata[j].sex = random.choice(
        [pyslim.INDIVIDUAL_TYPE_FEMALE, pyslim.INDIVIDUAL_TYPE_MALE])
    individual_metadata[j].age = random.choice([0, 1, 2, 3, 4])

pyslim.annotate_individual_metadata(tables, individual_metadata)
slim_ts = pyslim.load_tables(tables)
slim_ts.dump("recipe_16.9.trees")
```

As in section 16.8, we start by running a coalescent simulation with msprime, generating a tree sequence. We want to modify the individual metadata here, so at this point we need to switch to msprime's table representation with ts.dump_tables(), which unpacks the tree sequence into modifiable tables (tree sequences are immutable, for efficiency reasons, so modifications must be made to tables). We can then perform the default nonWF annotation on those tables using pyslim.annotate_defaults_tables(); this is parallel to our use of pyslim.annotate_defaults() in section 16.8. We then extract a list of individual metadata records from the tables, and loop through it setting random sexes and ages. (The age structure used here is just a placeholder for a more realistic distribution, of course.) Once the metadata records have been modified, they get loaded back into the tables, and then the tables get used to create a new SLiM-annotated tree sequence. Finally, the tree sequence gets written out to a `.trees` file. This is the typical workflow when modifying metadata: convert to tables, fetch the metadata from the tables, modify it, load it back into the tables, and finally recreate a tree sequence from the modified tables. This is necessary because the tree sequence is an immutable object, not designed to allow modification of this sort.

Having produced a `.trees` file from the script above, we can load it into a matching SLiM model and run, as we did before. For clarity, we'll leave every else the same about this model, so that the essential differences can be seen more easily:

```
initialize() {
    initializeSLiMModelType("nonWF");
    initializeTreeSeq();
    initializeSex("A");
    initializeMutationRate(0);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeMutationType("m2", 0.5, "f", 0.1);
    m2.convertToSubstitution=T;
    initializeGenomicElementType("g1", m2, 1.0);
    initializeGenomicElement(g1, 0, 1e8-1);
    initializeRecombinationRate(1e-8);
}
reproduction(NULL, "F") {
    subpop.addCrossed(individual, subpop.sampleIndividuals(1, sex="M"));
}
1 early() {
    sim.readFromPopulationFile("recipe_16.9.trees");
    target = sample(sim.subpopulations.genomes, 1);
    target.addNewDrawnMutation(m2, 10000);
}
early() {
    p0.fitnessScaling = 5000 / p0.individualCount;
}
1: late() {
    if (sim.mutationsOfType(m2).size() == 0) {
       print(sim.substitutions.size() ? "FIXED" else "LOST");
       sim.treeSeqOutput("recipe_16.9_II.trees");
       sim.simulationFinished();
    }
}
2000 { sim.simulationFinished(); }
```

Since this is a nonWF model, we have added a minimal `reproduction()` callback and an `early()` event that provides population regulation through density-dependence, as well as a call to `initializeSLiMModelType()` (see chapter 15 for discussion). Since it is a sexual model, we also added a call to `initializeSex()`. We want the model to terminate upon fixation or loss, as before, but in nonWF models mutations are not converted to substitutions automatically, so we add `m2.convertToSubstitution=T` to ensure that; of course we could just adapt the termination code to check the frequency of the introduced mutation instead. The rest of the model is unchanged, apart from filenames.

Note that the subpopulation loaded in from the `.trees` file is `p0`, not `p1`; `msprime` starts counting subpopulation IDs from zero. It is conventional in SLiM, in general, to number subpopulations from `p1`, but of course it doesn't really matter; it would be possible to reassign the subpopulation index before writing out the `.trees` file, but we do not do so here.

The only important caveat here is that the coalescent was not run with separate sexes, nor with overlapping generations, so it does not precisely reflect the dynamics involved in the non-neutral portion of the simulation. The coalescent is an approximation anyway; in fact, this would have been a concern in the previous recipe too, if exact Wright-Fisher dynamics were needed. Whether these sorts of deviations from exact SLiM dynamics are a concern or not will depend upon the nature of the analysis to be conducted downstream. If it is an issue, a further burn-in period could be run in SLiM with the correct dynamics, prior to introducing the sweep mutation; that burn-in would perhaps not need to be very long to wipe away any important traces of the incorrect burn-in dynamics (but it would be a good idea to confirm that with appropriate tests, of course). If absolutely exact dynamics are needed then the burn-in will have to be simulated in SLiM; that can still be done with tree-sequence recording with neutral mutations turned off, though, as in section 16.1, so it will still be much faster than a regular SLiM burn-in would have been.

When this model is run (an initial seed of 1661016094949 produces fixation in SLiM 3.1), we see the sweep occur and then a new `.trees` file is written out. We could conduct the same post-run analysis as before, printing out tree heights to verify that this burn-in procedure worked, but to avoid repetitiveness we will just end here. It is worth noting, in closing, that `pyslim` allows all sorts of annotation; it would be possible, with a similar strategy, to mark genomes as being X or Y chromosomes and then load them into a sex-chromosome simulation in SLiM, or to set the spatial positions of individuals before loading them into a spatial SLiM model, or whatever is needed. Of course, getting coalescent simulation results for such complex scenarios, even without any selected loci, may be a challenge.

16.10 Adding a neutral burn-in after simulation with recapitation

Very often, in forward genetic simulation, a "burn-in" period of neutral dynamics is desirable to allow the model to reach an equilibrium state of mutation–drift balance before non-neutral dynamics begin. Without a burn-in period, the pattern of neutral mutations observed at the end of the simulation may depend as much upon the initial state of the model as on the model's dynamics, which can make it difficult to interpret results. The modeling of this burn-in period is a persistent problem, however, because it is generally so time-consuming. An often-quoted rule of thumb is that the burn-in period should run for 10*N* generations – ten times the initial population size. For a model with 100,000 individuals, then, a million generations of burn-in is recommend, which – with such a large population size – will take an exceedingly long time. Worse, the 10*N* rule is often an underestimate of the time needed to equilibrate, particularly when simulating a very long chromosome; and there is no number of generations at which coalescence is guaranteed.

To cope with this issue, a wide variety of techniques are attempted. One might try to rescale the model during the burn-in period (see section 5.5), although this can introduce significant artifacts; or one might initialize the model with the output from a coalescent simulation (see sections 16.8 and 16.9); or one might run the burn-in period without neutral mutations, using tree-sequence recording to preserve the ancestry information that will allow them to be overlaid late (see sections 16.1 and 16.2). With SLiM 3.1, there is an option that is often better than any of these, which we will examine in this section: recapitation.

Recapitation is the addition of a neutral coalescent history to a simulation *after the fact*. The non-neutral portion of the simulation is run first, in SLiM, with tree-sequence recording enabled so that the genealogical history of all extant individuals is preserved. The result is saved to a `.trees` file, as in previous recipes. That `.trees` file is then loaded in Python, and msprime and pyslim are used to construct a coalescent history stretching back in time from the original ancestors of the simulation.

Enough discussion; let's see it in action. We will begin with a SLiM model of non-neutral dynamics, specifically a selective sweep:

```
initialize() {
    initializeTreeSeq(simplificationRatio=INF);
    initializeMutationRate(0);
    initializeMutationType("m2", 0.5, "f", 1.0);
    m2.convertToSubstitution = F;
    initializeGenomicElementType("g1", m2, 1);
    initializeGenomicElement(g1, 0, 1e6 - 1);
    initializeRecombinationRate(3e-10);
}
1 late() {
    sim.addSubpop("p1", 1e5);
}
100 late() {
    sample(p1.genomes, 1).addNewDrawnMutation(m2, 5e5);
}
100:10000 late() {
    mut = sim.mutationsOfType(m2);
    if (mut.size() != 1)
       stop(sim.generation + ": LOST");
    else if (sum(sim.mutationFrequencies(NULL, mut)) == 1.0)
    {
       sim.treeSeqOutput("recipe_16.10_decap.trees");
       sim.simulationFinished();
    }
}
```

This is a pretty typical tree-sequence-based model, with a mutation rate of zero. It involves a fairly large population size (`1e5`), and a reasonably long chromosome (`1e6`), so running the neutral burn-in for this model in SLiM would take quite a long time. Incidentally, the size of this simulation also means that simplification can take quite a long time, and so as well as recapitating, we have also chosen to speed up the simulation by setting the `simplificationRatio` parameter of `initializeTreeSeq()` to `INF`. We have not discussed the `simplificationRatio` option much before: in general, it controls how often simplification occurs, and a value specifically of `INF` tells SLiM not to simplify the tree sequence at all until a `.trees` file is generated (see section 21.1). Although this speeds up the model's execution considerably, it can greatly increase memory usage, so it should be done with care; it is easy to overflow the memory available to the process. As this particular example has a short runtime, we're probably safe to trade off memory to achieve maximum simulation speed, but for longer-running simulations you will probably want to tune the simplification interval as appropriate before recapitating.

This model involves a selective sweep, introduced in generation 100. We do not attempt to run this simulation conditional on fixation (see chapter 10); for simplicity, we just detect fixation or loss in the `100:10000 late()` event. On fixation, the model dumps a `.trees` file and stops.

So now, if we run the model until we get a run in which the sweep mutation fixes, we have a file named `recipe_16.10_decap.trees` that contains the genealogical history of that run. Now we run a Python script that performs the recapitation:

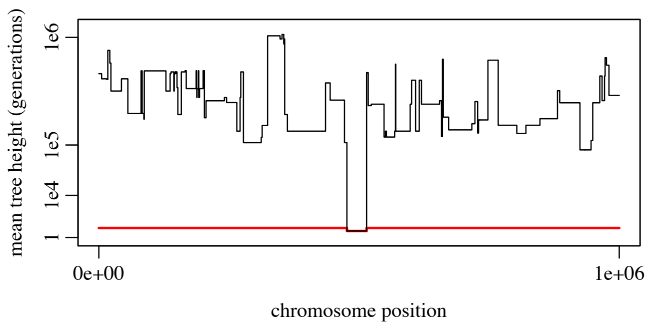
```
import msprime, pyslim
import numpy as np
import matplotlib.pyplot as plt
```

```
# Load the .trees file
ts = pyslim.load("recipe_16.10_decap.trees")    # no simplify!

# Calculate tree heights, giving uncoalesced sites the maximum time
def tree_heights(ts):
    heights = np.zeros(ts.num_trees + 1)
    for tree in ts.trees():
        if tree.num_roots > 1:  # not fully coalesced
            heights[tree.index] = ts.slim_generation
        else:
            children = tree.children(tree.root)
            real_root = tree.root if len(children) > 1 else children[0]
            heights[tree.index] = tree.time(real_root)
    heights[-1] = heights[-2]  # repeat the last entry for plotting
    return heights

# Plot tree heights before recapitation
breakpoints = list(ts.breakpoints())
heights = tree_heights(ts)
plt.step(breakpoints, heights, where='post')
plt.show()

# Recapitate!
recap = ts.recapitate(recombination_rate=3e-10, Ne=1e5, random_seed=1)
recap.dump("recipe_16.10_recap.trees")

# Plot the tree heights after recapitation
breakpoints = list(recap.breakpoints())
heights = tree_heights(recap)
plt.step(breakpoints, heights, where='post')
plt.show()
```

The first step is to load the `.trees` file. Note that we specifically do not call `simplify()` here, because we need the first generation individuals to recapitate from; this is, in fact, precisely why SLiM 3.1 preserves those individuals for us.

Then we define a function that calculates tree heights along the chromosome. This is similar to what we did in section 16.4, but here we have to be a bit smarter because of those original ancestors preserved in the tree sequence. Every tree will have a root in one of those original ancestors, but we are interested in whether the tree has coalesced below that original ancestor (and if so, at what height), or if the tree still has multiple roots, indicating that it has not yet coalesced.

We use that function to plot tree heights along the chromosome before recapitation. Then we recapitate, which is very easy – just a single method call on our tree sequence, returning a new tree sequence that has had a coalescent history traced backward from its original ancestors. The recapitation process just needs to know the recombination rate to use, and the population size (N_e) to use for the coalescent. Finally, we plot again, after recapitation, to see what it has done. A combined plot of these results, made in R, looks like this:



Note that the *y*-axis is rescaled according to the cube root of the number of generations, to bring out detail at both the low and high ends of the scale. The red line here shows the tree heights along the chromosome prior to recapitation. The area surrounding the sweep has coalesced at the generation in which the sweep mutation was introduced, due to strong hitchhiking in the vicinity of the mutation. The area further out has not coalesced, and therefore has a tree height that dates back to the beginning of forward simulation, 100 generations before the sweep began. The black line shows tree heights after recapitation; here the uncoalesced regions farther from the sweep have been coalesced backward in time as far as a million generations (reflecting the fact that we would have needed to run the burn-in in SLiM for at least a million generations to have any likelihood of coalescence). Regions closer to the sweep tend to coalesce more recently, reflecting the effect of the sweep on the diversity present at different regions along the chromosome at the end of simulation.

In short, we can see that recapitation has provided us with a full neutral burn-in history for the simulation, after the fact. Notably, this is very fast; this example run executed in 0.41 seconds. If we wanted neutral mutations overlaid over the whole population history, including the recapitated burn-in, that would also be extremely fast; using the technique shown in section 16.2, that operation would take another 0.58 seconds. These times can be compared to an estimate, obtained by extrapolation, of how long the burn-in would take in SLiM: more than 114 hours.

Recapitation, then, is optimal for computing burn-in for several reasons. One reason is that it is extremely fast, as we have seen; the only branches that need to be coalesced are those leading to the final individuals present at the end of forward simulation, which is generally a small minority of the branches that were present at the beginning of forward simulation. Recapitation is therefore much, much faster than simulating the burn-in period in SLiM, and should even be faster than constructing an initial population state with the coalescent; it is based upon the coalescent, but needs to do much less work since far fewer branches typically need to be coalesced. Then too, recapitation is very convenient, since it can be done after forward simulation, even as an afterthought on existing model output. In this way, it allows a focus on the non-neutral dynamics of interest, with burn-in handled later. It also allows one to ignore the question of how long to run burn-in for – the whole “10*N*” question – since recapitation will coalesce back in time as far as necessary to achieve full coalescence.

Of course, recapitation can only be used in scenarios where a neutral coalescent process is appropriate for burn-in. In some cases the burn-in period needs to itself be non-neutral; in this case using tree-sequence recording to run without neutral mutations may be the best one can do (see sections 16.1 and 16.2). But for many models, recapitation will enable modeling at a larger scale than previously possible, by greatly reducing the overhead of the burn-in period.

One point was glossed over in the discussion above: why was the sweep mutation introduced in generation 100, and not, say, in generation 2 immediately after the simulation has started? The easy answer is: to make the plot look nice. In the mean tree height plot above, there is a nice stairstep in the red line (showing mean tree height prior to recapitation), and that bump is there because of the delay between starting forward simulation and introducing the sweep mutation. But there is a deeper benefit as well: running a little bit of forward simulation after recapitation can smooth out differences introduced by the coalescent burn-in. The standard Kingman coalescent, as simulated here via the `recapitate()` command, produces evolutionary dynamics that are extremely similar to a neutral forward Wright–Fisher simulation such as the model shown above; but the two are not, in fact, exactly identical, and small differences introduced by the use of the coalescent could conceivably produce detectable bias in simulation results if non-neutral dynamics commenced immediately after the end of the coalescent. Doing a little extra neutral burn-in after the recapitated period shuffles things around so that any such bias is minimized.

Indeed, this technique can sometimes be used even to approximate a non-neutral burn-in period using the coalescent; one can forward-simulate the non-neutral burn-in dynamics in SLiM for some relatively short period of time (like 100 or 1000 generations), and then add a coalescent history to that using recapitation as a sort of convenient approximation to the truth. This is obviously not ideal; but if forward-simulating the full non-neutral burn-in period would take a prohibitively long time, it may be the only option available, and it may, for some models, prove to produce acceptable results. Of course any approximation like this should be carefully tested to ensure that any bias or artifacts introduced by it are within acceptable bounds.

17. Runtime control

In this chapter we'll look at topics related to what might be called "runtime control": manipulating the random number generator, saving simulation snapshots and data to files, executing "lambdas" as a way of making code dynamic and/or reusable, and debugging your models in SLiMgui. We will no longer be looking at complete recipes for models as we did in the previous chapters; instead, we will use shorter snippets of code to briefly explore a few topics likely to come up when you are developing models of your own.

17.1 The random number generator

We have encountered the (pseudo-)random number generator in various recipes, but it is worth focusing our attention on it briefly since random numbers are generally quite important for SLiM simulations.

SLiM and Eidos use a random number generator that is part of the GNU Scientific Library (GSL). More specifically, at present the GSL's `taus2` random number generator is used. It is possible to change this by modifying Eidos's internal code, but it is not recommended since Eidos and SLiM rely heavily on various properties of this generator, such as the number of random bits it outputs per draw, and the independence of the bits within each draw. It is a good generator with a long period, and should be suitable for most purposes. Starting in SLiM 3.0, a 64-bit Mersenne Twister generator is also used, for purposes where 64-bit random numbers are needed (since the `taus2` generator is only a 32-bit generator, but is significantly faster than the Mersenne Twister generator); the seeds of the two generators are synchronized, and the fact that there are two independent generators used under the hood should be essentially invisible to users of SLiM and Eidos; it can, for practical purposes, be considered a single generator.

The random number generator is seeded at the very beginning of each simulation run (each press of the Recycle button, in SLiMgui) using a combination of the current Un*x process ID and the clock time. This is not a particularly robust way to seed the generator; if you are doing production runs of a model, you will generally want to ensure that each run uses a different seed value. Perhaps the simplest way to ensure this is to pass a seed value to SLiM on the command line via the `-seed` or `-s` option; for example:

```
slim -seed 12345 ./script.txt
```

If you write a Un*x script (or an R script, or whatever) to launch all of your SLiM model runs, that script can use this command-line option to set up each model run with a distinct seed value.

Within the code for a model, it is also possible to manipulate the random number generator's seed value; the recipe in section 10.2 did this in order to re-run the model from the same starting point with different seeds, for example. The `getSeed()` function returns the last seed value set, and the `setSeed()` function sets a new seed value. Note that calling `setSeed(getSeed())` generally changes the state of the random number generator; the seed returned by `getSeed()` is the last seed value set to initiate a random sequence, but since random numbers may have been generated since that seed was set, the seed does not necessarily reflect the current state of the generator.

The recipe of section 10.2, and some other recipes in the cookbook, change the random number seed with a particular formula:

```
setSeed(rdunif(1, 0, asInteger(2^32) - 1));
```

This is a useful way to change to a new seed (allowing the subsequent run to be reproduced directly by starting at the saved simulation point with the same new seed value) while still preserving a dependency upon the original seed value. These recipes used to do setSeed(getSeed() + 1)) instead, but that could be problematic if a set of replicate runs are done using sequential initial seed values; the replicate run starting with seed 1 will graduate to successive seeds of 2, 3, etc., and will thus end up using exactly the same pseudorandom sequence as the replicate runs that started with (or graduated to) those higher seed values. Since the identical pseudorandom sequences would be used in conjunction with a different simulation state, it *might* not end up mattering; but there is no point in taking the risk of accidental correlation between runs, so it is best to follow this new strategy, which should avoid this issue. (Thanks to Matthew Hartfield for pointing this out.) The rdunif() call generates a seed within the unsigned 32-bit range of the taus2 generator; values outside this range would still work (they are taken modulo 2^{32} anyway), but this range makes the intent of the code clear.

When running a SLiM model, the seed value set when the simulation is initialized is automatically printed to the output. For example, you might see:

```
// Initial random seed:
1455193095666
```

If a particular model run catches your interest and you wish to reproduce it, you can copy that initial seed value and add a statement to the beginning of your model's initialize() callback like:

```
setSeed(1455193095666);
```

If you recycle the model after adding such a line, you will see a different initial seed value printed; but after you step over the initialize() phase, you should see the model repeat its previous sequence, because the different initial seed value was replaced by the setSeed() call.

17.2 Defining constants on the command-line

It is common to want to run a model many times, perhaps varying some of the basic parameters that define the model, or perhaps just varying the random number seed in a predictable way in order to produce independent replicates of the simulation. To make this simpler, SLiM provides a command-line option, -define (or just -d) that allows you to specify definitions for Eidos constants that your script can then use. For example, consider this simple script:

```
initialize() {
    setSeed(seed);
    initializeMutationRate(mu);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(r);
}
1 {
    sim.addSubpop("p1", N);
}
2000 late() { sim.outputFixedMutations(); }
```

This is just a simple neutral drift model, as we have used for the basis of many recipes in this cookbook. However, it references four undefined variables: the random number seed seed, the mutation rate mu, the recombination rate r, and the population size N. Run "as is", the script would therefore fail with an "undefined identifier" error.

But when invoking this model at the command line, these values can be defined as Eidos constants using the -d command-line option. Assuming that slim and the script test_defines.txt are at findable paths, this would be an example invocation of the model:

```
slim -d seed=7 -d mu=1e-7 -d r=1e-8 -d N=500 test_defines.txt
```

The values would then be defined and available to the script. (Note that setting the random number seed at the command line can also be achieved with the `-seed` command-line option; see section 17.1). With this mechanism, it is easy to set up a script that runs a large number of slim jobs on a computing cluster, for example, to produce replicated runs across a whole parameter space. A call to `cat()` at the beginning of your script could output the values for all of the constants defined externally, so that the output from each run of SLiM is marked with the parameter values that generated it.

Incidentally, one might wish to write the above model such that the final generation depends upon the defined value of `N`; it is common, for example, to run a neutral burn-in period for 10*N* generations (although this practice is not without problems). It would be nice to be able to write:

```
10*N late() { sim.outputFixedMutations(); }
```

Unfortunately, this does not work; the generation range for script blocks must use simple `integer` constants. (This is difficult to fix because "constants" like `N` are not, in fact, necessarily constant – they can be removed with `rm()` and redefined – and because the values of constants may not be known at the time the script is parsed, such as when they are defined with `defineConstant()`.) Instead, the standard "trick" is to define the script block with a symbol, like this:

```
s1 2000 late() { sim.outputFixedMutations(); }
```

The symbol `s1` now refers to this script block. Then the script block can easily be rescheduled to the desired generation (or generation range) using the `rescheduleScriptBlock()` method, as in this rewritten generation `1` `early()` event:

```
1 {
    sim.addSubpop("p1", N);
    sim.rescheduleScriptBlock(s1, start=10*N, end=10*N);
}
```

The `s1` event will now run in generation `10*N` as desired. Note that the generation declared for `s1` – `2000`, here – is no longer important, since s1 will be rescheduled anyway. The only caveat is that the declared generation should be *after* the generation in which the rescheduling occurs, to ensure that `s1` does not get executed before the rescheduling takes place. See section 22.1 for further discussion on the declaration of event script blocks.

One might wish to supply constants definitions in this manner when running at the command line, but have the model still run properly under SLiMgui, with default values for constants, rather than producing an "undefined identifier" error. Here is a version of the `initialize()` callback for the above model that achieves this:

```
initialize() {
    if (exists("slimgui"))
    {
       defineConstant("seed", 1);
       defineConstant("mu", 1e-7);
       defineConstant("r", 1e-8);
       defineConstant("N", 1000);
    }

    setSeed(seed);
    initializeMutationRate(mu);
```

```
        initializeMutationType("m1", 0.5, "f", 0.0);
        initializeGenomicElementType("g1", m1, 1.0);
        initializeGenomicElement(g1, 0, 99999);
        initializeRecombinationRate(r);
    }
```

The `slimgui` object, which provides an Eidos interface to SLiMgui (see section 21.11), is defined only when running under SLiMgui, so the constants will be defined only in that case.

One could similarly use `exists()` to test for the existence of each constant, and define their values only if they are undefined; this would allow the model to run at the command line with no `-d` definitions supplied, using default values, but would allow those default values to be overridden with a `-d` command-line flag when desired. For example, this defines `seed` only if it has not already been supplied:

```
    if (!exists("seed"))
        defineConstant("seed", 1);
```

Defined constants can be of type `logical`, `integer`, `float`, or `string`; defining `string` constants probably requires playing quoting games with your Un*x shell, such as:

```
    slim -d "foo='bar'" test.txt
```

The fact that Eidos strings such as `'bar'` can be enclosed in either single or double quotes comes in useful here. If the `-l[ong]` command-line option is supplied (turning on more verbose output from SLiM), the argument for each `-d[efine]` command-line option will be printed as it was received by SLiM after processing by the shell, making it somewhat simpler to diagnose quoting issues.

In fact, the values for defined constants can be any Eidos expression, and can even reference previously defined constants. For example, one may accomplish scaling of model parameters by the population size with an invocation such as:

```
    slim -d N=1000 -d THETA=5 -d "mu=THETA/(4*N)" model.txt
```

Here the mutation rate `mu` is calculated from the population size `N` and the scaled model parameter `THETA`. Note that with such expressions, as with `string` literals, quoting is probably necessary to avoid issues with your Un*x command shell, as shown above. Expressions of any kind are allowed, including calls to Eidos functions, and the result of the expression need not be a singleton. The random number generator will be initialized (with the supplied `-seed` value, if any; see section 17.1) before the command-line definition expressions are evaluated, so functions that rely upon random numbers will use values based upon the model's initial seed.

It is a good idea to use unique names for defined constants that do not collide with any symbols defined by Eidos or SLiM. Some such names will be flagged as errors; others, such as collisions with the names of pseudo-parameters that SLiM provides to callbacks, may just cause confusion. You might wish to employ a naming convention for your constants to avoid all possibility of collisions, such as using names that begin with `d_`.

See section 13.8 for an example of using this feature with ABC-MCMC parameter estimation.

17.3 Other command-line options

Previous sections have touched upon a few of the command-line options for SLiM. In particular, section 17.1 showed how to pass a seed for the random number generator using the `-s` or `-seed` option, and section 17.2 showed how to define Eidos constants on the command line with the `-d` or `-define` option. There are a few other commend-line options supported by SLiM, which we will briefly summarize here.

First of all, there are options that are not related to running simulations. The `-v` or `-version` option prints out the version number of the slim executable you are using:

```
$ slim -v
SLiM version 3.2, built Nov  6 2018 09:41:03
```

The `-u` or `-usage` option causes SLiM to print out a summary of how it can be invoked on the command line (i.e., more or less the same information we're summarizing here), in case you forget an option and want a quick reminder.

The `-testEidos` or `-te` option makes SLiM run a self-test of the Eidos language interpreter. Similarly, the `-testSLiM` or `-ts` option runs a self-test of the SLiM core. Typically you would use these after building SLiM to verify that the built executable is functioning properly (see section 2.4):

```
$ slim -te
SUCCESS count: 5439
$ slim -ts
SUCCESS count: 68424
```

The success counts are not important, and will depend upon the version of SLiM being run; the important thing is that no failed tests are reported.

Then there are command-line options that influence a simulation run in some way. Setting the random number seed with the `-s` / `-seed` option, and defining Eidos constants at the command line with the `-d` / `-define` option, have already been discussed; several other options also exist.

The `-l` or `-long` option enables "long" output, which provides additional information about the run. At the moment this is primarily useful for getting information about mutation run usage (see section 18.4); other long output may be added in future.

The `-t` or `-time` option enables output of the total runtime of the simulation (see section 18.2). When this option is enabled, a final line will be printed showing the CPU usage of the process (in seconds), like:

```
// ********** CPU time used: 0.11412
```

The `-m` or `-mem` option similarly enables output about the memory usage of the simulation (see section 18.3). When this option is enabled, final lines will be printed showing the initial and peak memory usage of the simulation (in bytes, K, and MB), like:

```
// ********** Initial memory usage: 1069056 bytes (1044K, 1.01953MB)
// ********** Peak memory usage: 4325376 bytes (4224K, 4.125MB)
```

The `-M` or `-Memhist` option provides more extensive output regarding the memory usage of the process as it runs, in the form of a final dump of usage statistics encapsulated within R code that can be copied and pasted into an R interpreter to produce a plot of memory usage over time (see section 18.3). This is not likely to be useful to end users; it is mostly a tool for debugging SLiM itself.

The `-x` option disables some of SLiM's runtime checks for consistency and safety. It is not recommended for general use, since it may mean that error conditions are not caught and reported. However, it may occasionally be useful if one of SLiM's runtime checks is actually faulty and needs to be disabled (see section 18.3).

When running a simulation, the path to the SLiM script file is typically supplied at the end of the command line. After SLiM 3.2, this may be omitted if a script file is instead piped in to SLiM's standard input ("stdin", in Un*x parlance). In other words, this invocation of SLiM:

```
$ slim ~/Desktop/foo.slim
```

may instead be written as:

```
$ cat ~/Desktop/foo.slim | slim
```

This allows the input script to be assembled dynamically (in Python, say) and passed to SLiM via stdin, without having to create a temporary script file on disk to pass to SLiM.

17.4 File input and output

Output generated by a simulation with `print()`, `cat()`, and similar output functions goes into SLiM's output stream, which (assuming you are running at the command line) can be redirected to a file to save the results of the model run. Often, however, you will want a model to explicitly write output to a file. Eidos provides a few simple functions for file input and output, as well as operators and functions for string manipulation, and SLiM adds to those capabilities with some model-specific output functions. It should be possible for you to use these facilities to achieve whatever sort of customized output you wish; it is trivial, for example, to output information about the current state of a model as a comma-separated value (CSV) file that can be read by R and other such software in order to perform further analysis.

The simplest way to output simulation state to a file is to use the `SLiMSim` method `outputFull()`, such as by calling:

```
sim.outputFull("~/model_output.txt");
```

This produces a population dump in a standard format that is compatible with the `SLiMSim` method `readFromPopulationFile()`; these two methods can thus be used to save and restore the population state at any point in time, as discussed further in section 10.2.

But suppose this standard output format is not suitable; instead, you want to save a CSV file with a list of all of the mutations currently active in the simulation, listing their positions and selection coefficients. A recipe to achieve that might look like:

```
lines = NULL;
for (mut in sim.mutations)
{
    mutLine = paste(c(mut.position, ", ", mut.selectionCoeff, "\n"), "");
    lines = c(lines, mutLine);
}
file = paste(lines, "");
file = "position, selcoeff\n" + file;
if (!writeFile("~/out.txt", file))
    stop("Error writing file.");
```

This recipe assembles a vector of output lines, naturally called lines, starting with `NULL` and adding new lines with `c(lines, mutLine)`. A `for` loop is used to loop over all the mutations in the simulation, and for each mutation an output line is assembled using `paste()`. Each line ends with a newline pasted on to the end with `"\n"`.

After the `for` loop, the next line uses `paste()` to join all of the lines produced by the loop into a single string, and the following line prepends a header line with column names for the output. At this point, `file` contains the string to be written to a file in the filesystem. Writing it out is achieved simply by calling `writeFile()`, passing the filesystem path for the first parameter and the string to write as the second. The `writeFile()` function returns a logical value: `T` if the file was written successfully, or `F` if a filesystem error occurred. It is a good idea to check the return value, as shown here, so that you are aware if your model's output is not working as expected.

The recipe above will work fine, but the use of the `for` loop is quite inefficient and is not true Eidos style; Eidos is a vectorized language, and it is generally better to use vectorized solutions when possible. Similarly, assembling a long vector with a series of `c()` calls to add one element at a time is highly inefficient in Eidos, requiring memory allocation and bulk copying of data with each successive addition. A better recipe to achieve the same result, then, would be:

```
lines = sapply(sim.mutations, "paste(c(applyValue.position, ', ',
                applyValue.selectionCoeff, '\\n'), '');");
file = paste(lines, "");
file = "position, selcoeff\n" + file;
if (!writeFile("~/out.txt", file))
    stop("Error writing file.");
```

The first statement (wrapped onto two lines in the code shown above, but entered as a single line of code without the newline in the middle of the `string` literal) uses the `sapply()` function to assemble a vector containing `string` output lines for each mutation in the simulation. Conceptually, this is similar to the `for` loop across `sim.mutations` in the previous example, with `applyValue` as the index variable for the loop, and executing the Eidos code within `sapply()`'s second parameter as the `for` loop's body. However, `sapply()` also collects the result of each iteration of the loop and assembles all of those results in a single vector, here assigned into the variable `lines`; it thus does the work that `lines = NULL` and `c(lines, mutLine)` did above, but *much* more efficiently. The `sapply()` function is immensely useful for bulk processing of data, and should become a part of every Eidos programmer's toolbox; it is documented in detail in the Eidos manual.

Note that because we want the code executed by `sapply()` to paste a newline at the end of each line using the escape sequence `\n`, we have to escape the backslash; `\\n` in the original code becomes `\n` in the `string` literal representing the code run by `sapply()`, which becomes a newline in the `string` literal passed to `paste()`. Similarly, the double-quoted parameters to `paste()` in the first version of the recipe are now single-quoted, allowing the quotes to nest without escaping issues. Confusing, yes; section 17.5 below will show a different approach that may be clearer and easier.

17.5 Lambda execution

A few recipes have touched on the ability of Eidos to execute code that was dynamically assembled as a string. For example, section 10.5.3 added new script blocks to the running simulation to schedule future mutation events, and section 17.4 passed a string representing an executable code block to the `sapply()` function. Such dynamic execution of code is a relatively advanced technique, but can be very powerful.

The first step in this technique is simply to assemble a string containing the Eidos code you wish to execute. This is generally done with the + operator, which performs string concatenation when given at least one `string` operand, and the `paste()` function, which pastes together a vector of strings joined by a fixed separator string. Sometimes, as in section 17.4, the string can even just be a literal; this technique does not necessarily involve dynamically generated code. Usually the main difficulties in this step involve correct escaping of special characters, and the related issue of quoting and nested quotes. The fact that Eidos allows strings to be quoted with either single or double quotes can be helpful; see, for example, the way that section 17.4 avoids having to escape quote characters by using single quotes inside the double-quoted code string. Another useful technique for handling quoting and escaping difficulties is the so-called "here document" style of string literal in Eidos (a terrible term, which I did not invent), documented in the Eidos manual. For example, section 17.4 used a small snippet of code:

```
lines = sapply(sim.mutations, "paste(c(applyValue.position, ', ',
                 applyValue.selectionCoeff, '\\n'), '');");
```

This could be rewritten with the "here document" style as:

```
lines = sapply(sim.mutations, <<---
paste(c(applyValue.position, ", ", applyValue.selectionCoeff, "\n"), "");
>>---);
```

Note that double quotes can now be used without any escaping issues, and that the newline escape sequence desired in the `string` literal can be given directly as `\n`, without the necessity of quoting it as `\\n` to prevent an actual newline character from being inserted in the `string`. It is worth getting used to the "here document" `string` literal style; it will simplify your life tremendously if you work with Eidos code as `string` literals.

In any case, once the code `string` in this example is assembled, it is passed to `sapply()`, and `sapply()` treats it as Eidos code – the `string` gets tokenized, parsed, and interpreted just as the literal code in your model's script is tokenized, parsed, and interpreted. The `sapply()` function is one of several functions in Eidos that executes a `string` as code in this manner; another is the `executeLambda()` function, which simply executes the `string` it is passed as code. This can be used, to some extent, in a similar way to how functions are used in many other programming languages, but with a more dynamic twist. For example, suppose we wanted to write code that performed an operation on pairs of operands – but we don't know what operation we want to perform ahead of time. It might be addition, subtraction, multiplication, division, or exponentiation; all we have is a `string` indicating the desired operation. Without `executeLambda()`, we would have to write:

```
[... code that sets up operand1, operand2, and operator somehow ...]

if (operator == "+")
     result = operand1 + operand2;
else if (operator == "-")
     result = operand1 - operand2;
else if (operator == "*")
     result = operand1 * operand2;
else if (operator == "/")
     result = operand1 / operand2;
else if (operator == "^")
     result = operand1 ^ operand2;
```

With `executeLambda()`, this becomes trivial:

```
[... code that sets up operand1, operand2, and operator somehow ...]

result = executeLambda(paste(c("operand1", operator, "operand2;")));
```

This is a rather contrived example, admittedly, but such situations do arise from time to time; it is worth being aware of this facility.

SLiM leverages this facility in Eidos to allow you to add new script blocks to a simulation dynamically, with code that can be assembled dynamically as a `string` and passed in to the SLiM engine. Both Eidos events and callbacks can be added, using the `SLiMSim` methods `registerEarlyEvent()`, `registerLateEvent()`, `registerFitnessCallback()`, `registerMateChoiceCallback()`, `registerModifyChildCallback()`, and `registerRecombinationCallback()`.

17.6 Debugging

One of the weaker points of the Eidos language at present is its facilities for debugging. There is no runtime debugger for Eidos, no ability to pause executing code at an arbitrary point in order to examine variables, no breakpoints or watchpoints. However, Eidos does nevertheless have some facilities for debugging that you should be aware of.

The first is simply the ability to print to the output console at any point in your code. If you are wondering whether a calculation you have written produces the correct value, simply add a call to `print()` or `cat()` to see the value in the output. This is primitive, admittedly, but still powerful, and in fact is often quicker and simpler to produce an answer than a debugger would be.

The variable browser, opened with the Show Eidos Variable Browser button in SLiMgui's main window, is a useful debugging facility. This is described in section 3.4, and is quite useful since it can browse into SLiM's state as well as your own variables. Unfortunately it can only show you the state of things in between generations; there is no way to pause while inside the execution of a `fitness()` callback, say, and browse the variables at that moment in time. Nevertheless, it is a powerful tool.

The console window, opened with the Show Eidos Console button in SLiMgui's main window, provides a third debugging facility. This is described in section 3.3. In the console window, you can work with Eidos interactively, defining your own variables and executing your own code. All of SLiM's top-level variables are available to you in the console, so you can test out code that manipulates genomes and mutations and so forth. If you set up some dummy variables with the same names that SLiM uses in callbacks (such as `mut`, `homozygous`, `relFitness`, etc., for a `fitness()` callback), you can test out your callback code interactively in the console. It's not quite the same as working in a debugger, but it's not bad. Note that all of the variables you define in the console are visible in the variable browser, too. You can even use the console window to change the state of the running SLiM simulation; code executed in the console is executed in the same Eidos context as the simulation to which the console is attached.

Often the help documentation, available through the Script Help button ?, is an overlooked tool for debugging. If your code isn't doing what you think it should do, often the best approach is to examine your underlying assumptions: is your mental model correct regarding all of the objects, methods, properties, functions, etc., used by your code? There is a reason why `RTFM` is often the first debugging advice given by experienced programmers. The help window is documented further in section 3.2.

A key step in debugging is often to find a reproducible case. A bug that crops up rarely and unpredictably can be terribly hard to track down; a bug that you can make happen over and over, while examining it from different angles, is usually much more tractable. In SLiM, since so much of what happens is usually guided by the random number generator, using `setSeed()` to make a simulation follow the same path in each run is often an important step in debugging. See section 17.1 for more information on working with the random number generator.

Debugging is never easy; it is detective work, often reminiscent of the thought process advocated by Sherlock Holmes: eliminate hypotheses one by one until only one possibility remains, and that must be the answer. Good luck!

18. Implementation and performance

Following the lead of the previous chapter, this chapter will also present shorter snippets of Eidos code, rather than complete models, to illustrate selected topics in model development. In this chapter, we will focus on topics related to technical considerations in model implementation and performance: speed, memory usage, and evaluation of performance.

18.1 Writing fast SLiM simulations

Evolutionary simulations are often limited not by ideas (there are always lots of interesting questions to explore), and not by the difficulty of writing the models to test those ideas (especially when using tools such as SLiM and Eidos that facilitate that process), but rather by time and processing power. Individual-based modeling is computationally intensive, and since it is generally not practical to spend years of computer time on a single problem, it often becomes necessary to limit the scope of one's investigation. Naturally this is undesirable, and so squeezing every last bit of speed out of one's simulation is beneficial; it may allow you to ask a broader question, or explore a larger parameter space, or use a larger population size.

When using a high-level modeling framework like SLiM, the most important thing in gaining high performance is to understand the design of the framework; often there are different ways to solve the same problem that provide vastly different performance. For example, SLiM allows you to define a `fitness()` callback with an optional subpopulation constraint. Without using that optional constraint, you might write:

```
fitness(m2) {
    if (subpop == p2)
      return 0.5;
    else
      return relFitness;
}
```

Using the optional constraint feature, you would instead write:

```
fitness(m2, p2) {
    return 0.5;
}
```

These are identical in their behavior, but the second version will perform orders of magnitude (literally) better than the first version. There are a bunch of reasons for this. The first version requires that the `fitness()` callback be called for every mutation in every subpopulation, rather than just for the mutations in subpopulation `p2`, and the setup and teardown costs for running a callback are non-trivial, so that in itself has a large impact. Looking up the values of variables such as `relFitness` and `subpop` is also time-consuming. Doing the `(subpop == p2)` test in interpreted Eidos code is vastly slower than doing the same test internally in SLiM, since SLiM's core code is compiled and optimized C++. Even beyond all of those considerations, however, there is also the fact that the second callback above is specifically optimized by SLiM: a callback that does nothing except return a constant value gets short-circuited by SLiM's internal machinery completely. In that case, there is no setup and teardown for an Eidos interpreter to run the callback, because there is no interpreted execution of the callback's code at all; SLiM is smart enough to know to simply use the value `0.5` for the relative fitness in the cases where that callback would execute. The same optimization cannot be done for the first version.

To some extent, these sorts of implementation details of the SLiM engine are private and should not be relied upon; they might change from version to version of SLiM. But an overall take-home point is clear: whenever possible, write as little Eidos code as possible, and let the internals of SLiM and Eidos do as much work for you as possible.

There are lots of other examples of this principle. For example, you should use the vectorized facilities of Eidos whenever possible. To add a bunch of numbers, use one call to `sum()`, not a `for` loop performing sequential addition with the `+` operator. Similarly, to perform some repetitive operation on every element of a vector, consider using `sapply()` instead of a `for` loop. If the repetitive operation involves a conditional – if you're considering writing a `for` loop with an `if` statement inside it – consider using `ifelse()` instead (or at least, again, using `sapply()`). In general, it is safe to say that whenever you start writing a `for` loop in Eidos you should stop and ask yourself, "Can this be vectorized instead?"

Another example is the problem of looking up mutations of a given type in SLiM. Often you want to get a list of all mutations in the simulation that are of type `m2` (for example). To do this, the natural Eidos idiom, as in R, would be to subset with a `logical` vector, like:

```
muts = sim.mutations[sim.mutations.mutationType == m2];
```

To execute this statement for a simulation with N active mutations, Eidos must (1) fetch the `mutations` property from `sim`, assembling a vector of size N, (2) fetch the `mutationType` property of that vector, constructing a new vector with size N, (3) do an `==` comparison with `m2`, constructing a `logical` vector of size N, (4) fetch the `mutations` property from `sim` a second time, again assembling a vector of size N, and (6) do a size-N subset operation with the `[]` operator, using the two vectors constructed in the previous steps, to produce the final result. This is a huge amount of work, often to construct a result vector that might have just one element in it (since often the mutation type of interest involves a single introduced mutation). Precisely because this is such a common task, SLiM provides a shortcut:

```
muts = sim.mutationsOfType(m2);
```

Conceptually, this does the same thing as the previous version, but it does it in C++, inside SLiM's internal code, and that allows it to be orders of magnitude faster. When SLiM offers you facilities like this, use them! On SLiMSim, another such method is `countOfMutationsOfType()`, which is even faster than taking the `size()` of the result of `mutationsOfType()` if you just need to know how many there are without getting the objects themselves. Similar methods exist on some other SLiM classes, such as `Genome`.

Eidos itself also has quite a few such time-saving functions, from standard fare like `min()` and `max()` to more esoteric functions like `cumProduct()`, `unique()`, and `sapply()`. Indeed, most of the functions defined by Eidos are technically unnecessary; the tasks they perform could be written in pure Eidos code without the use of any functions. Eidos nevertheless provides you with a large library of predefined functions, for convenience, clarity, reuse, and speed; learn and use this toolkit. If you find yourself writing out some operation in lengthy and inefficient Eidos code, it might be time to take a step back and ask whether some or all of that operation could be recast in terms of built-in Eidos functions. Some Eidos functions, such as `which()` and `sapply()`, take some effort to learn to use effectively, but the payoff is large.

Another performance consideration is that defining and looking up variables in Eidos code is relatively slow. This is not an issue most of the time, but in code that gets executed a lot (a `fitness()` callback on a common mutation type, for example) it can make a large difference. Using variables to represent temporary, intermediate computations can make code much easier to understand, but unfortunately it can also run much more slowly. For example, consider this code to compute the Euclidean distance between two points, `(x1,y1)` and `(x2,y2)`, and execute some code only if that distance is less than a constant threshold distance:

```
    dx = x1 - x2;
    dx_sq = dx * dx;
    dy = y1 - y2;
    dy_sq = dy * dy;
    dist = sqrt(dx_sq + dy_sq);
    if (dist < 4.0)
        ...
```

Don't do that unless you don't care at all how slowly it runs (which often is true – optimize only when you need to optimize). Instead, if you care about speed, do this:

```
    if (sqrt((x1 - x2)^2 + (y1 - y2)^2) < 4.0)
        ...
```

Sometimes, of course, defining a temporary variable can improve performance, if the temporary value is used more than once. If the value of that Euclidean distance computation will be used more than once, then by all means assign it into a variable; looking up variable values may be slow, but it's not nearly as slow as performing a complex, multistep calculation. But at least avoid defining the temporary variables `dx`, `dx_sq`, `dy`, and `dy_sq` if those values are used only once.

Of course it also pays to actually think about the necessity of the calculations you're performing. In the above example, there is actually no point to calculating the square root; instead, you can just compare the square of the distance to the square of the threshold:

```
    if ((x1 - x2)^2 + (y1 - y2)^2 < 16.0)
        ...
```

Learning to see such opportunities for optimization is largely a matter of patiently and methodically examining each line of your code to think about how steps might be folded together or eliminated entirely. A few hours of such effort might save you weeks or months of runtime.

These tips provide some general approaches and rules of thumb for improving simulation performance. The following sections will discuss more concrete tools that can be brought to bear.

18.2 Performance evaluation

Sometimes you want to know exactly how long a piece of code or a whole simulation takes to run; this can be useful when trying to optimize the performance of a model, for example, for comparing alternative formulations of the model quantitatively. SLiM and Eidos provide several tools for this purpose. See section 18.5, on profiling simulations in SLiMgui, for another extremely useful tool for performance evaluation.

First of all, to measure the total execution time of an entire simulation run on the command line, you can pass the command-line option `-time` or `-t` to SLiM and it will print a total time measurement to the output at the end of the run. The same facility is not presently offered in SLiMgui, since production runs are generally done at the command line, and the time taken in SLiM may not accurately reflect the time that will be taken in a command-line run, given the overhead of user-interface updating. When using the `-time` option, keep in mind that a given model may exhibit a wide variance in execution time depending upon the random number sequence used by a run; comparing runs using a fixed random number seed is therefore wise. See section 17.1 for details on using `-seed` or `setSeed()` to set up a reproducible model run.

If you want to measure the performance of Eidos code or even a whole SLiM model, the `clock()` function can also be a good way to go. This function returns the amount of CPU time used by the running process; the difference between the result of clock() at one point versus another point is thus the amount of CPU time that was used between the two points. Measuring a single chunk of code is therefore trivial:

```
start = clock();
for (i in 1:100000)
    q = i;
cat("Elapsed: " + (clock() - start));
```

Measuring the performance of code that spans multiple code blocks (such as the full execution time of a SLiM model) is just a little more complicated, because the start variable would not be persistent for long enough. Using the `defineConstant()` function of Eidos to store the start time fixes that problem. So in the `initialize()` callback of your model, you could put this:

```
defineConstant("start", clock());
```

And then in a `late()` event in the final generation, you could write:

```
cat("Elapsed: " + (clock() - start));
```

The elapsed time printed is in seconds, but not of user (i.e. wall-clock) time; rather, it is in CPU time (the amount of time your computer's processor actually dedicated to running the model, which might be much less than the wall-clock time, particularly if your computer is busy doing other things as well).

For measuring the performance of just a small block of code, the `executeLambda()` function has a timing option that can also be useful. Just pass `T` as the second, optional parameter to `executeLambda()` and it will print a time measurement for the lambda. For example, suppose we wanted to measure the time it takes to execute this code:

```
mean(runif(10000000) * 10);
```

We could simply execute it inside an `executeLambda()` call, like so:

```
executeLambda("mean(runif(10000000) * 10);", T);
```

On my machine, this produces this output:

```
// ********** executeLambda() elapsed time: 1.07904
5.00037
```

The return value of the call is `5.00037`, and running the lambda took `1.07904` seconds. Supposing that to be unacceptable, we could try a simple optimization, changing the range of the `runif()` call, which draws random deviates from a uniform distribution, rather than reshaping the drawn values with multiplication afterwards. Since we're drawing ten million values, it is reasonable to wonder whether this might make a difference, so let's try it:

```
executeLambda("mean(runif(10000000, 0, 10));", T);
```

This produces this output:

```
// ********** executeLambda() elapsed time: 0.644127
4.99945
```

So incorporating the scaling into the `runif()` call sped up the code by about a third; not bad. The final result in the two cases is different, of course, because the random number generator is not in the same state; you could use `setSeed()` to do tests with identical random number sequences if you wished, but it should be irrelevant in this case.

Section 17.5 has further advice about how to use the `executeLambda()` function, including a discussion of the "here document" `string` literal style, which makes it much less painful to convert Eidos code into the form of a `string` literal that can be passed to `executeLambda()`.

Section 18.5 provides an overview of profiling simulations in SLiMgui, which – for users on Mac OS X – provides a particularly useful way of evaluating simulation performance.

18.3 Memory usage considerations

Sometimes memory usage is a major concern when running individual-based simulations. SLiM has been engineered to keep its memory usage relatively low, but simulations involving large population sizes and large numbers of mutations can burn through megabytes and even gigabytes of memory. Reducing memory usage can be difficult, unless you are willing to change the parameters of your simulation, but it is at least possible to assess SLiM's memory usage.

Several tools are provided to assess SLiM's *total* memory usage, including SLiM's code, operating system overhead, and so forth. The first tool is the `–mem` or `–m` command-line option, which causes SLiM to keep track of the high-water mark of its memory usage and print out that high-water mark when the model finishes. The second tool is the `–Memhist` or `–M` command-line option, which causes SLiM to track and print the memory usage of the simulation over time, rather than just the high-water mark. A third tool is the Eidos function `usage()`, which returns the current or peak memory usage of the running process, in megabytes (MB).

To get more detail about SLiM's internal memory usage, the `outputUsage()` method of `SLiMSim` can be called at any time to get a breakdown of the current memory usage by the simulation (see section 21.12.2), and in SLiMgui the same information is available in profile reports (see section 18.6). These facilities do not assess SLiM's *total* memory usage; instead, they provide a detailed picture of the memory that SLiM itself allocates and has direct control over. For large simulations this should be the large majority of total memory usage, however, so this should not prove limiting in practice. These features are covered in more detail in section 18.6.

It is usually the case that the large majority of the memory used by SLiM is for the references kept by `Genome` objects to the `Mutation` objects that the genomes contain (by `MutationRun` objects, internally, beginning in SLiM 2.4, but those objects are not visible to the user of SLiM; see section 18.4). Genomes refer to mutations using 32-bit indexes (4 bytes), for memory efficiency (pointers, by comparison, are typically 64-bits, or 8 bytes, on modern systems). A single genome containing 1000 mutations thus takes about 4K of memory, a diploid individual with that mutational density would take ~8K, and a population of 1000 such individuals would take ~8MB (although if shared haplotypes were common that overhead might be reduced by `MutationRun`'s ability to share mutation references between genomes). It is easy to see that with very large population sizes or very large numbers of active mutations the memory overhead becomes quite large (particularly if genetic diversity is high so that haplotype sharing is minimal). This overhead is more or less unavoidable, since a genome simply must keep a list of the mutations it contains; there would be possible ways to compress the memory footprint of that list, but such schemes would inevitably make SLiM much slower. If your simulation is taking too much memory, you typically really have only a few options: (1) make your population size and/or chromosome size smaller, (2) change your model to have a lower mean number of active mutations per genome (modeling fewer background neutral mutations, for example – or none at all, as tree-sequence recording can allow; see section 1.7), (3) change your model to have more haplotype sharing (with a lower recombination rate, for example), or (4) buy more memory.

Note that, interestingly, it is the references to the mutations that burn the memory, in most typical simulations, not the `Mutation` objects themselves. This is because in a typical simulation one mutation is often contained by a large number of individual genomes. A single `Mutation` object presently takes up 80 bytes on OS X (implementation details like this are of course subject to change). If a single reference to that `Mutation` object takes 4 bytes, as we saw above, then once 20 genomes contain that mutation, the memory footprint of the references is already as large as the footprint of the `Mutation` object itself. A mutation near fixation in a population of only 1000 diploid individuals would use the same 80 bytes for the `Mutation` object, but 4*1000*2 = 8K bytes for the references to the object (again, potentially reduced by haplotype sharing through MutationRun). That footprint is so large that all other memory usage is typically irrelevant.

Beginning in SLiM 2.1, runtime checks of SLiM's memory usage are performed periodically, if and only if SLiM is running under a process memory limit (as indicated by the results of the Un*x function `getrlimit()`). Such memory limits are often enforced for jobs running on computing clusters, and exceeding the limits causes immediate termination of the process by the operating system. To make such memory overflow terminations easier to debug, SLiM will print a diagnostic message if its memory usage approaches within 10 MB of the limit, stating what SLiM was doing when the overflow occurred; if the operating system kills the process soon after that point, this diagnostic message may prove useful for determining the problem. This runtime checking should not add significant performance overhead to SLiM, but it can be disabled with the `-x` command-line flag if so desired. Note that some systems will report that there is no memory limit, even when a limit is actually in force, so this feature may or may not work on a given system.

18.4 Mutation runs and runtime optimization

Beginning in SLiM version 2.4, a change was made to SLiM's core engine. With this change, each genome in the simulation can be broken into multiple "mutation runs", each of which contains the mutations that occur within a given subsection of the genome. A simulation might use four mutation runs per genome, for example, in which case every genome is divided into four roughly equal-sized chunks – the mutation runs – that are stored separately. This is an internal implementation detail that is not visible to SLiM models in Eidos, and normally it is of no concern. However, in some circumstances an awareness of the existence of mutation runs can allow a model to be optimized to run faster than it otherwise would.

The purpose of mutation runs is to allow some operations performed by SLiM to be performed faster than they otherwise could be. For example, suppose a gamete needs to be produced by recombination of the two parental genomes, and a single recombination breakpoint has been drawn. Without mutation runs, generating the gamete would require copying all of the mutation pointers from the first parental genome up to the breakpoint, and then copying all of the mutation pointers from the second parental genome from the breakpoint onward; if a typical genome contains 1000 mutations, generating a gamete will require copying 1000 pointers. Now suppose the genomes are divided into 10 mutation runs each. The breakpoint occurs inside one of those 10 runs, and mutation pointers will need to be copied from the parental mutation runs for those; that will be about 100 pointer copies. But for the other nine runs – this is the crucial bit – only the pointer to the mutation run itself needs to be copied to the gamete, because the gamete can share the mutation runs with other genomes. That makes 109 pointer copies total – a big improvement on 1000. Similar gains can be realized in other parts of the SLiM core engine as well. Using mutation runs adds in some bookkeeping overhead, but it usually at least breaks even in terms of performance, and often it results in a substantial speedup. It also improves memory usage, since long runs of pointers to mutation objects can be shared among many genomes.

The tricky question is: how many mutation runs should be used? If too few are used, then most of the benefits evaporate. If too many are used, SLiM spends most of its time just handling the bookkeeping involved; if every genome contains 1000 mutation runs, there are now 1000 times more objects involved in the simulation than there were, with immense performance implications.

Choosing the right number of mutation runs to use can thus be very important; the performance of the simulation can change dramatically depending upon this value. Unfortunately, there is no general way to make this choice; factors such as the chromosome length, mutation rate, and population size are important, but so are things like population dynamics, the type of selection being experienced, and the effects of custom Eidos events and callbacks in the SLiM script.

In order to manage this problem, SLiM 2.4 and later actually conducts little experiments continuously: it times every generation, while occasionally varying the number of mutation runs being used. As it collects datasets, it compares those datasets against each other (using *t*-tests, in fact!) to determine how many mutation runs is optimal. These experiments take very little time, and run continuously in the background. This means that the end user of SLiM usually doesn't have to think about all of this; the optimal number of mutation runs is used most of the time, and simulations run a little bit (or a lot) faster with no effort on the part of the user. It also means that if simulation dynamics change partway through – perhaps a neutral burn-in ends and a regime of strong selection begins – SLiM will notice the changed dynamics and automatically adjust the number of mutation runs to be optimal in each part of the simulation.

So far, so good. However, all of these experiments do have a small effect on performance. This can be particularly true for models for which the optimal number of mutation runs is not clear or changes frequently, as well as models with a very short generation time. Sometimes, telling SLiM to use a fixed number of mutation runs can be beneficial – but you need to know how many.

As an example, let's look at a very simple neutral model:

```
initialize() {
    initializeMutationRate(1e-5);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 1e5-1);
    initializeRecombinationRate(1e-5);
}
1 { sim.addSubpop("p1", 500); }
10000 late() { sim.outputFixedMutations(); }
```

In SLiM 2.3, this model takes approximately 205 seconds to run (on my machine). In SLiM 2.4, if a single mutation run is used, this model runs in approximately 77 seconds, thanks to other performance optimizations added to version 2.4. If 32 mutations are used in SLiM 2.4, on the other hand, it runs in approximately 24 seconds – more than three times faster! As it happens, 32 is the optimum for this model, for most of its runtime (a small number of runs is better early on, when neutral diversity is still building). Actually, the optimum might be different in a different hardware/software environment (things like how much processor cache memory is available can be very important), so to be precise, 32 is the optimum on my machine at the present moment.

Running the model in SLiM 2.4 with no mutation run count specified, and therefore allowing SLiM to perform its "experiments" continuously in the background, results in a runtime of 30 seconds, with 78.5% of the generations in the simulation using 32 mutation runs (in one trial run; this will vary from run to run, even with the same random number seed, since it depends upon timing information). SLiM therefore does a reasonably good job of finding the optimum, but telling it explicitly to use 32 mutation runs rather than conducting experiments results in even better performance – about a 20% speedup.

So in practice, how could we arrive at this result? The first step is to run the model at the command line with a few extra command-line options:

```
$ ./slim -m -t -l -s 0 ~/neutral.slim
```

This command runs, at the `$` prompt in my Un*x terminal, the `slim` executable in the current directory (`.`), executing the model named `neutral.slim` in my home directory (`~`). The "`-s 0`" option tells SLiM to use a random number seed of `0` (see section 17.1); I chose this so that all of my test runs use exactly the same modeled sequence of events, which you may or may not want to do as well. The "`-m`" flag turns on memory monitoring (see section 18.3), and the "`-t`" flag turns on timing of the overall runtime (see section 18.2); that is how I collected the timing information given above. Finally, the "`-l`" flag (short for "`-long`", which may be used instead) tells SLiM to output long (i.e., verbose) output. Exactly what gets added to verbose output is version-specific (so try not to make assumptions about it, and probably don't use it in your production model runs), but one of the things added is information about the mutation run experiments conducted by SLiM. When the model finishes executing, among the verbose output is a snippet like this:

```
// Mutation run modal count: 32 (78.5% of generations)
//
// It might (or might not) speed up your model to add a call to:
//
//    initializeSLiMOptions(mutationRuns=32);
//
// to your initialize() callback.  The optimal value will change
// if your model changes.  See the SLiM manual for more details.
```

This tells us what we want to know: 32 is the optimal mutation run count for this model. Again, that is on this hardware in the present software environment; if you plan to do your production runs on a computing cluster, for example, you should ascertain the optimal mutation run count on the cluster – ideally when it is busy running other tasks on its other cores – since the optimum there may be different than on your local machine. (Note that similar, and even more detailed, information on mutation run usage can be obtained in SLiMgui using its profiling feature; see section 18.5. However, this might or might not indicate the optimum number of mutation runs for command-line runs, since the runtime environment for SLiM is somewhat different when it is running inside SLiMgui. The above method using the `-l` command-line flag is therefore recommended.)

Knowing that 32 is the optimal mutation run count, we can now modify our model as the output above suggests by adding an `initializeSLiMOptions()` configuration call at the beginning of the `initialize()` callback that tells SLiM how many mutation runs to use (see section 21.1):

```
initializeSLiMOptions(mutationRuns=32);
```

This will yield the desired 20% speedup, because SLiM will no longer conduct mutation run experiments, and will instead simply use 32 mutation runs throughout the model's execution.

Note that in some cases this could actually make a model perform worse! Earlier, for example, we mentioned the possibility of a model involving a neutral burn-in period followed by a period of strong selection. The optimal number of mutation runs might be very different in those two phases of the model – 64 in the first half and 1 in the second half, say – but if SLiM is conducting its own mutation run experiments, it should be able to adjust to that fact. If you specify a fixed number of runs, however, then either the first half or the second half of the model might perform quite poorly. It is not possible to change the number of mutation runs dynamically in Eidos, at present, so in such cases the best option is to allow SLiM to run its experiments and do its runtime optimization. Such cases can be detected simply by looking at the total runtime of the model with and without a specified number of mutation runs; if specifying the number of runs makes the model run more slowly, then you probably shouldn't do it.

In summary, the ability to specify the mutation run count is an advanced feature, the correct use of which requires some experimentation and careful timing using the appropriate hardware and software. If done properly, however, it can produce performance gains of as much as 20%, or probably even more for some models. For very large models with long runtimes, it is therefore an important tool.

18.5 Profiling simulations in SLiMgui

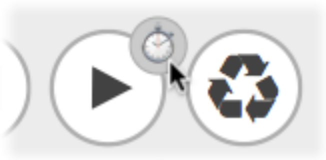
The previous sections have provided some pointers and tips regarding measuring and optimizing the memory usage and performance of a SLiM model. For users on Mac OS X, SLiMgui provides a particularly useful performance tool, called *profiling*, beginning in SLiM version 2.4.

For the purposes of this section, we will reuse the recipe from section 12.4, which shows how to use a `modifyChild()` callback to disable incidental selfing in hermaphroditic models (defined as occurring when the same individual happens to be chosen for both the first and second parent in a biparental mating event). Note that this recipe has been deprecated, since there is now a configuration flag for SLiM that disables incidental selfing more easily and efficiently (see section 12.4). Nevertheless, this recipe still works, and is a good one for our purposes here:

```
initialize() {
    initializeMutationRate(1e-7);
    initializeMutationType("m1", 0.5, "f", 0.0);
    initializeGenomicElementType("g1", m1, 1.0);
    initializeGenomicElement(g1, 0, 99999);
    initializeRecombinationRate(1e-8);
}
1 { sim.addSubpop("p1", 500); }
modifyChild()
{
    // prevent hermaphroditic selfing
    if (parent1 == parent2)
       return F;
    return T;
}
10000 late() { sim.outputFixedMutations(); }
```

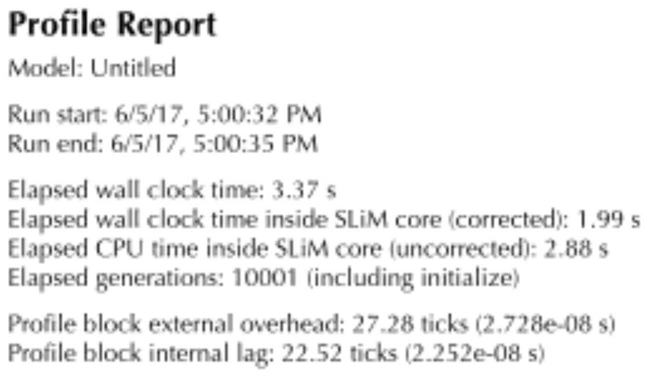
This is a very simple neutral simulation; the only twist is the `modifyChild()` callback that checks whether the two parents of the focal offspring are the same, and if so, rejects the offspring by returning `F`. The recipe has been changed here to run for `10000` generations, to provide more accurate measurements that are more focused on the steady state of the model rather than its initialization.

To profile this model in SLiMgui, simply click the profiling button that is overlaid with the play button in the SLiMgui main window:



This will play the simulation forward from the current generation, just as the Play button would; the only difference is that SLiMgui will tabulate performance information about the simulation while it is running. You can start profiling at any point in a simulation run; for example, you can play up to the generation in which a critical section of your model begins, and then profile from there onward. Similarly, you can stop profiling at any time by clicking the profiling button again; you do not need to wait for the model run to complete. When the current profiling operation completes, a new window opens that shows a profile report. This report contains several sections; we will discuss them one by one.

The first section is the report header:



Profile Report

Model: Untitled

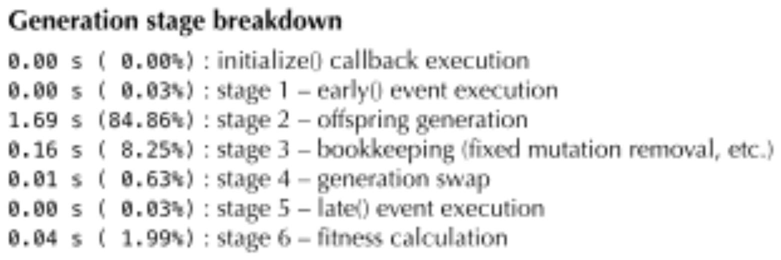
Run start: 6/5/17, 5:00:32 PM
Run end: 6/5/17, 5:00:35 PM

Elapsed wall clock time: 3.37 s
Elapsed wall clock time inside SLiM core (corrected): 1.99 s
Elapsed CPU time inside SLiM core (uncorrected): 2.88 s
Elapsed generations: 10001 (including initialize)

Profile block external overhead: 27.28 ticks (2.728e-08 s)
Profile block internal lag: 22.52 ticks (2.252e-08 s)

The header contains general information: the title of the model, when the profiling run began and ended, and some overall timing and memory usage information. (i) The first "wall clock time" listed is the actual time spent running the model in SLiMgui; in this case, 3.37 seconds. (ii) The second wall clock time is time spent inside SLiM's core code; this excludes time spent in SLiMgui, doing things like updating the user interface. It is also stated to be "corrected"; what this means is that an attempt has been made to subtract out time spent inside the profiling code itself, reading the system clock and tabulating profiling results. This number is thus SLiMgui's best guess as to how long the model would take if it were run at the command line with the `slim` command instead. Since this is the runtime that is generally of interest, it is used as a baseline in the profile report; later in the report, when timing percentages are reported, they are always percentages out of this correct wall clock time. (iii) Third comes the elapsed CPU time inside the SLiM core; CPU time is time spent keeping the processor of the computer busy. This time can be quite different from the other times reported, as it is here. On the one hand, it excludes time spent in SLiMgui, so it is generally lower than the total elapsed wall clock time. On the other hand, it is uncorrected – it does not exclude time spent inside the profiling code itself – so it is typically longer than the corrected wall clock time. And then, too, CPU time is often different from wall clock times anyway, particularly if your machine is busy with other tasks that are also occupying the processor. (Incidentally, to obtain optimal profiling results it is a good idea to quit all other applications and run the profile when your machine is otherwise completely idle.) (iv) Next is shown the number of generations over which the profile ran, including the initialization phase of the model. (v) Finally, two lines profile information about the measured overhead and lag of the profiling code; these numbers are used to produce the corrected wall clock time, and are not generally of interest to end users of SLiMgui. (Note that in SLiM 3.2 another two lines were added at the end, providing information about SLiM's overall memory usage; these will be discussed in the next section.)

The next section is the "Generation stage breakdown":

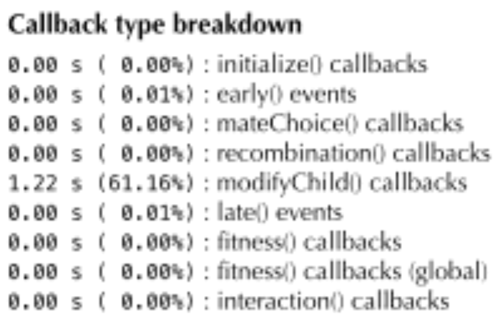


Generation stage breakdown

```
0.00 s ( 0.00%) : initialize() callback execution
0.00 s ( 0.03%) : stage 1 – early() event execution
1.69 s (84.86%) : stage 2 – offspring generation
0.16 s ( 8.25%) : stage 3 – bookkeeping (fixed mutation removal, etc.)
0.01 s ( 0.63%) : stage 4 – generation swap
0.00 s ( 0.03%) : stage 5 – late() event execution
0.04 s ( 1.99%) : stage 6 – fitness calculation
```

This is a tabulation of where SLiM is spending its time, broken down according to generation stage. The fact that 84.86% of SLiM's time is being spent in offspring generation is a red flag; that generation stage does often take quite a bit of time, but not typically this much. So this is something to note – depending upon the model it is not necessarily an indication of a problem, but it is certainly an indication of where you ought to focus your optimization efforts.

Next is the "Callback type breakdown" section:

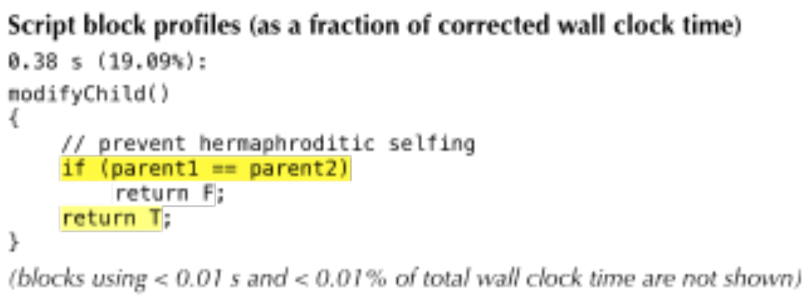


Callback type breakdown

```
0.00 s ( 0.00%) : initialize() callbacks
0.00 s ( 0.01%) : early() events
0.00 s ( 0.00%) : mateChoice() callbacks
0.00 s ( 0.00%) : recombination() callbacks
1.22 s (61.16%) : modifyChild() callbacks
0.00 s ( 0.01%) : late() events
0.00 s ( 0.00%) : fitness() callbacks
0.00 s ( 0.00%) : fitness() callbacks (global)
0.00 s ( 0.00%) : interaction() callbacks
```

This section shows a tabulation of where SLiM is spending its time, broken down according to callback types. This does not add up to 100% because SLiM is spending almost 40% of its time outside of callbacks, in the SLiM core engine. But it is spending 61.16% of its time inside `modifyChild()` callbacks – again, an indication of where to focus optimization efforts. You might also wonder why 61.16% is different from 84.86%. This is because the additional time, above 61.16%, is being spent by SLiM in offspring generation, but not inside `modifyChild()` callbacks. This time would be spent doing mutation generation and recombination, for example.

The next section is titled "Script block profiles (as a fraction of corrected wall clock time)":



Script block profiles (as a fraction of corrected wall clock time)

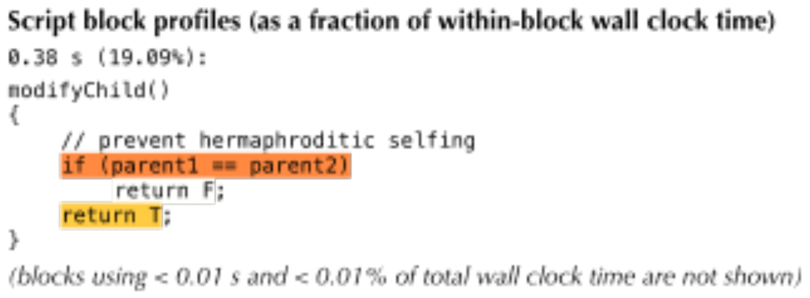
```
0.38 s (19.09%):
modifyChild()
{
	// prevent hermaphroditic selfing
	if (parent1 == parent2)
		return F;
	return T;
}
```

(blocks using < 0.01 s and < 0.01% of total wall clock time are not shown)

This shows the model's code, with color highlighting indicating where time is being spent. Colors range from white (essentially no time spent here) through yellow and up to orange and finally red (most of the simulation's time spent here). This section colors the code according to the time spent as a fraction of the total corrected wall clock time. We can see that the `modifyChild()` callback is taking 19.09% of SLiM's time, and two parts of it are responsible: the test for the two parents being identical, and the returning of `T` to indicate that the child should be generated. The callback does occasionally return `F`, but that is so rare that that line is more or less white. Again you might wonder: why is 19.09% different from 61.16%? The reason is that 19.09% is spent specifically on interpreting the lines of code inside the callback – inside the Eidos interpreter – whereas 61.16% is spent overall on calling the callback. Calling out to callbacks involves a certain amount of overhead in SLiM; the Eidos interpreter environment for the callback must be set up, variable values for it must be initialized, and so forth. The difference between 19.09% and 61.16% reflects all of this overhead. The overhead is very high in this case because the callback is so simple; the more complex a callback's code is, the less this constant overhead will matter. But in this case, the profile report is telling us that it is not so much the callback's code that is hurting us – it is the fact that we have a callback at all.

Note, by the way, that only the `modifyChild()` script block is shown here. As the italic comment at the bottom of the section notes, only script blocks that take more than a certain amount of time are shown, since script blocks that take a tiny fraction of the total time are generally not of interest from an optimization perspective.

Following that section is "Script block profiles (as a fraction of within-block wall clock time)":



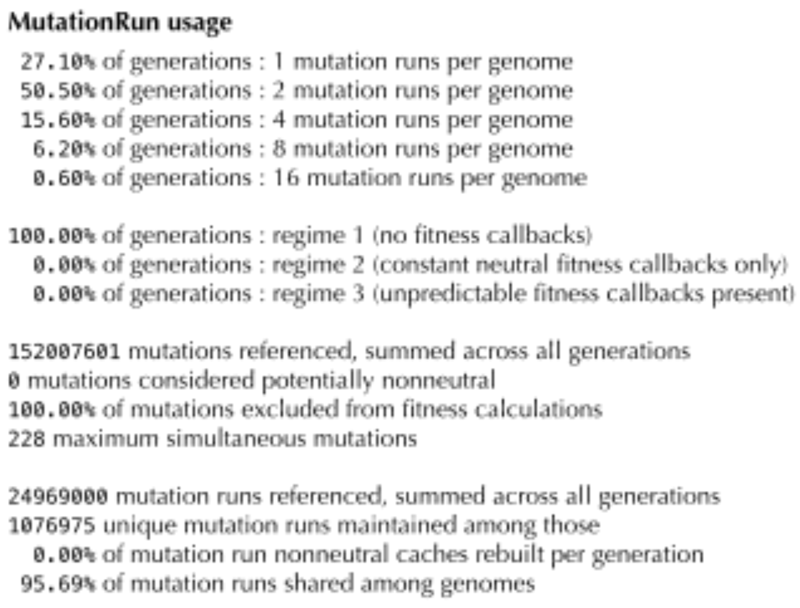
Script block profiles (as a fraction of within-block wall clock time)

```
0.38 s (19.09%):
modifyChild()
{
    // prevent hermaphroditic selfing
    if (parent1 == parent2)
        return F;
    return T;
}
```

(blocks using < 0.01 s and < 0.01% of total wall clock time are not shown)

This section shows a similar view of the model's code, but here the colors are scaled to the time spent within each block. Even a block that takes up almost none of the total time, therefore, will show "hotspots" that may be close to red. Here the two hotspot lines we noticed before are colored orange, but the first line is a darker shade, closer to red, indicating that it takes more time than the second line. This can also be seen in the shades of yellow used in the previous section of the report, but it is much more subtle; the point of this section, with colors according to within-block time, is precisely this, to increase the visibility of the hotspot lines. However, this section is usually of less interest than the previous section, since the proportion of the total corrected wall clock time is what ultimately matters.

Finally, the last section is "MutationRun usage":

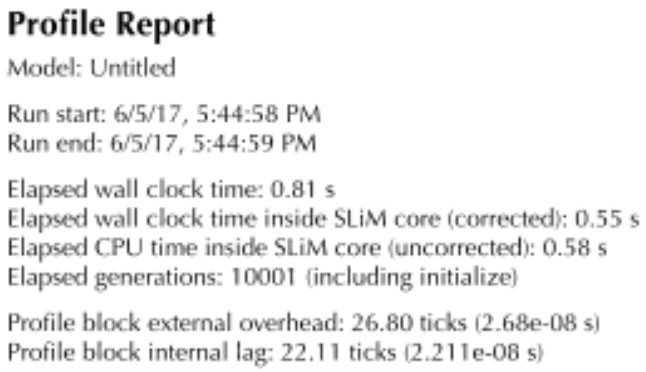


MutationRun usage

```
 27.10% of generations : 1 mutation runs per genome
 50.50% of generations : 2 mutation runs per genome
 15.60% of generations : 4 mutation runs per genome
  6.20% of generations : 8 mutation runs per genome
  0.60% of generations : 16 mutation runs per genome

100.00% of generations : regime 1 (no fitness callbacks)
  0.00% of generations : regime 2 (constant neutral fitness callbacks only)
  0.00% of generations : regime 3 (unpredictable fitness callbacks present)

152007601 mutations referenced, summed across all generations
0 mutations considered potentially nonneutral
100.00% of mutations excluded from fitness calculations
228 maximum simultaneous mutations

24969000 mutation runs referenced, summed across all generations
1076975 unique mutation runs maintained among those
  0.00% of mutation run nonneutral caches rebuilt per generation
 95.69% of mutation runs shared among genomes
```

This section contains fairly technical information about some of SLiM's internal bookkeeping mechanisms, such as mutation runs and their caching of fitness-related information. Section 18.4 of this manual describes the basic idea behind mutation runs, and so may shed some light on the meaning of this section. Mostly, however, it is intended for internal use by the developers of SLiM (the royal we, in other words). If you send us a profile report from your simulation, this section will help us diagnose the situation. We will not discuss this section further here.

Overall, this report focuses our attention very clearly on the source of the performance problem with this model: the `modifyChild()` callback. Happily, as section 12.4 discusses, we can eliminate that callback now with a call to `initializeSLiMOptions(preventIncidentalSelfing=T)`, which sets a configuration option that causes SLiM to block incidental selfing internally instead. If we add that call to the model, remove the `modifyChild()` callback, and profile the model again, the header of the report now looks like this:



Profile Report

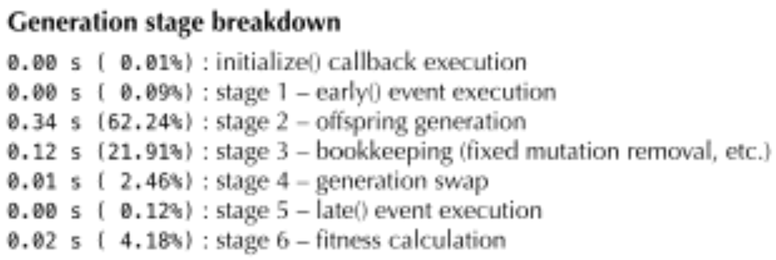
Model: Untitled

Run start: 6/5/17, 5:44:58 PM
Run end: 6/5/17, 5:44:59 PM

Elapsed wall clock time: 0.81 s
Elapsed wall clock time inside SLiM core (corrected): 0.55 s
Elapsed CPU time inside SLiM core (uncorrected): 0.58 s
Elapsed generations: 10001 (including initialize)

Profile block external overhead: 26.80 ticks (2.68e-08 s)
Profile block internal lag: 22.11 ticks (2.211e-08 s)

The total runtime is much shorter now – 0.55 seconds of corrected wall clock time inside the SLiM core, instead of 1.99 seconds! If we look at the generation stage breakdown, it now shows a healthier mix of time spent in various generation stages; the runtime is no longer being completely dominated by one stage:

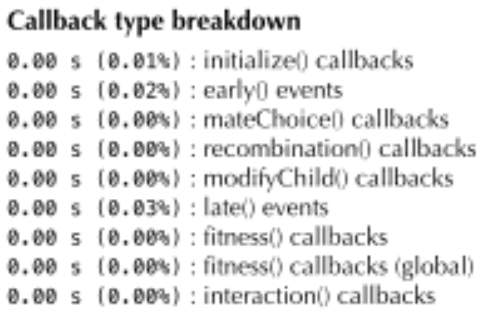


Generation stage breakdown

```
0.00 s ( 0.01%) : initialize() callback execution
0.00 s ( 0.09%) : stage 1 – early() event execution
0.34 s (62.24%) : stage 2 – offspring generation
0.12 s (21.91%) : stage 3 – bookkeeping (fixed mutation removal, etc.)
0.01 s ( 2.46%) : stage 4 – generation swap
0.00 s ( 0.12%) : stage 5 – late() event execution
0.02 s ( 4.18%) : stage 6 – fitness calculation
```

Offspring generation is now 62.24% instead of 84.86%, so SLiM is busy doing other things too; and even more encouraging, the total time spent in offspring generation is now 0.34 seconds instead of 1.69 seconds, so we have shaved off quite a bit of the actual time spent.

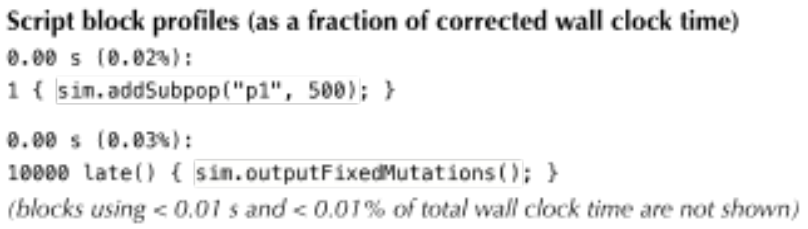
The callback type breakdown shows that we are now spending a negligible amount of time in callbacks:


Callback type breakdown

```
0.00 s (0.01%) : initialize() callbacks
0.00 s (0.02%) : early() events
0.00 s (0.00%) : mateChoice() callbacks
0.00 s (0.00%) : recombination() callbacks
0.00 s (0.00%) : modifyChild() callbacks
0.00 s (0.03%) : late() events
0.00 s (0.00%) : fitness() callbacks
0.00 s (0.00%) : fitness() callbacks (global)
0.00 s (0.00%) : interaction() callbacks
```

None is over 0.03% of the total time, so they are all basically irrelevant. What this says is that SLiM is no longer spending a significant amount of time inside the model's Eidos callbacks; virtually all of the time is being spent inside the SLiM core. If you still wanted to make this model faster, you would therefore have to decrease SLiM's core workload, by doing things like reducing the population size, reducing the recombination rate or mutation rate, etc. If such revisions to the model are not possible, then the model might be running about as fast as it possibly can (assuming there are no design flaws in the model causing it to waste time).

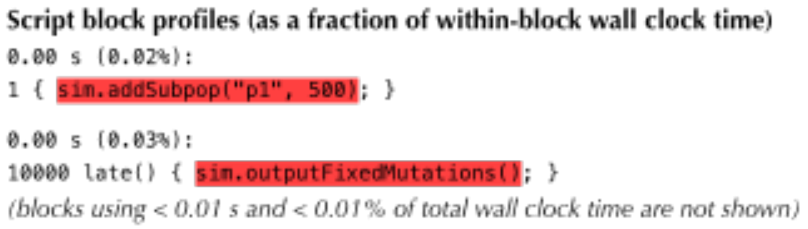
The first script block profile section confirms this; there are no hotspots in the code at all:


Script block profiles (as a fraction of corrected wall clock time)

```
0.00 s (0.02%):
1 { sim.addSubpop("p1", 500); }

0.00 s (0.03%):
10000 late() { sim.outputFixedMutations(); }
```
(blocks using < 0.01 s and < 0.01% of total wall clock time are not shown)

Two script blocks are now shown that weren't shown before, since they are now over the threshold to be listed; but they take 0.03% or less of the total time.

The second script block profile section shows some red hotspots:


Script block profiles (as a fraction of within-block wall clock time)

```
0.00 s (0.02%):
1 { sim.addSubpop("p1", 500); }

0.00 s (0.03%):
10000 late() { sim.outputFixedMutations(); }
```
(blocks using < 0.01 s and < 0.01% of total wall clock time are not shown)

Remember, however, that in this section the coloring indicates the time spent as a fraction of the within-block time. These lines might be taking 100% of the within-block time; indeed, they could hardly fail to do so, since each block is only one line long! But the fact remains that their fraction of the total runtime is inconsequential, so they should be ignored.

Particularly perspicacious readers may have noticed that if the original model took 1.99 seconds, 61.16% of which was dealing with `modifyChild()` callbacks, one might expect the modified model to take 0.77 seconds, but in fact it took only 0.58 seconds, so we got an even larger speedup than expected. Why is this? The main reason is probably that when callbacks are present, SLiM is often forced to take a slower code path, which adds runtime even beyond the overhead of handling the callbacks themselves. When `modifyChild()` callbacks are in force, for example, SLiM has to generate children in a random order, to eliminate possible order-dependency bugs that could otherwise crop up. When no such callbacks are active, SLiM can generate offspring in a fixed order – females before males, migrants before residents, etc. – which is substantially faster since it doesn't require randomization.

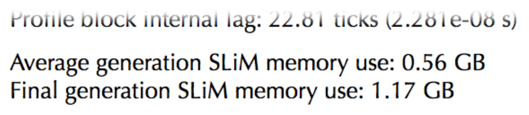
All of this might prompt the question: "OK, I've got all this profile information, so what?" Well, in some cases it might allow you to see a way to modify your model to avoid the hotspot in question; if your profile showed that you were spending an inordinate amount of time doing addition in a `for` loop, for example, you might question why you are doing so much addition, and whether you could use `sum()` instead – or whether perhaps you don't need to do all that addition at all. Eidos also provides quite a few functions that can perform various tasks very quickly; using functions like `unique()`, `setSymmetricDifference()`, `which()`, and so forth can lead to much faster code than attempting to code such logic in Eidos by hand.

In other cases, it will allow you to start a conversation with us about the performance problem you're seeing; if you say "I've got this model and it's spending 80% of its time inside the `mateChoice()` callback running the second `for` loop, what can I do about that?" that's a much better starting point than "My model is slow, help". If you are having to perform a multistep algorithm in Eidos for a task that is common, we might be able to add a new utility method to SLiM to perform this task for you with a single call. This can often result in a big speedup for the code in question, and it benefits all of SLiM's users for such utility methods to exist. The `sumOfMutationsOfType()` method, for example, was added in response to a performance-related question from a SLiM user, and is now available to speed up a wide variety of QTL-based models that need to calculate the additive effects of all mutations of a given type.

18.6 Profiling memory usage in SLiMgui, or with `outputUsage()`

The previous section introduced SLiMgui's profiling feature, with an extended example showing how it can be useful for improving the runtime of a simulation. Beginning in SLiM 3.2, the profiling feature has been extended to include information about memory usage as well; we will discuss that extension in this section. Note that sections 18.3 and 18.4 cover some important ideas about SLiM's memory usage; you may wish to read those sections first.

First of all, when running SLiM 3.2 or later the header section of a profile report will be a bit longer due to a subsection added at the end. For a somewhat large spatial simulation with tree-sequence recording enabled, the report might show something like this:

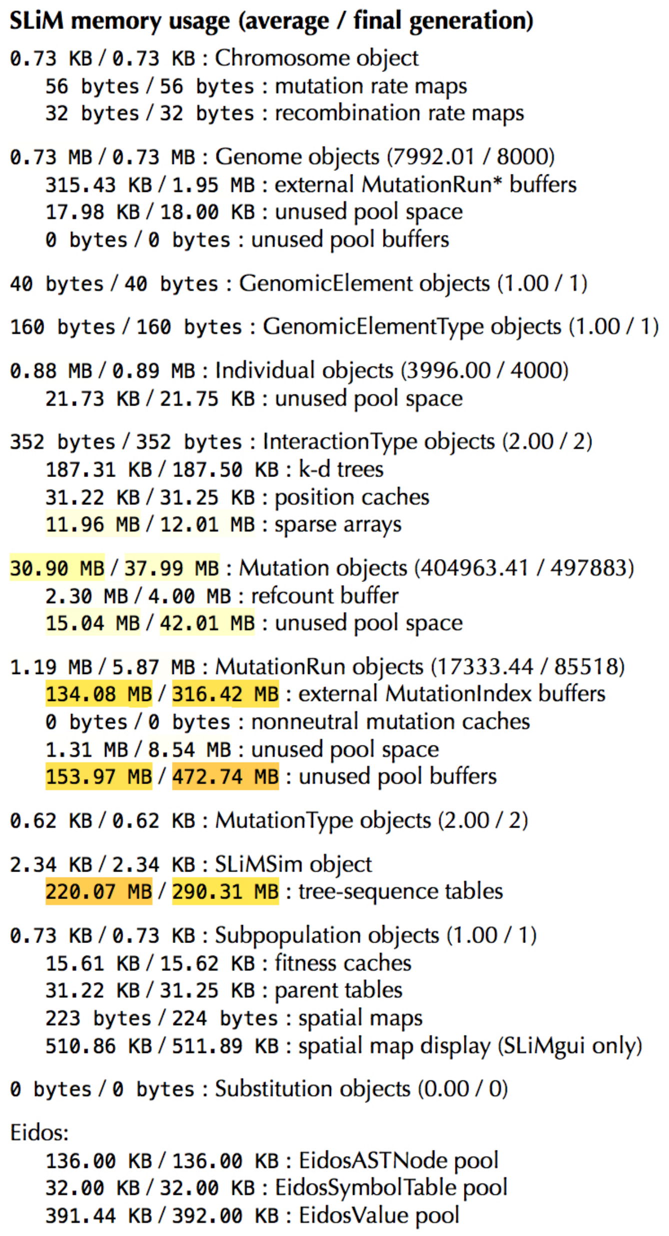


```
Profile block internal lag: 22.81 ticks (2.281e-08 s)

Average generation SLiM memory use: 0.56 GB
Final generation SLiM memory use: 1.17 GB
```

These lines report statistics about SLiM's overall memory usage. The first line gives the *average* usage, across a samples taken once per generation during the profiling period. The second line gives the sampled usage in the final generation profiled. Note that these memory usage samples are always taken at the end of each generation; if memory usage spikes within a generation but decreases again before the generation's end that will not be reflected in any of the profiling statistics discussed in this section (but *would* be captured by the overall usage statistics discussed in section 18.3). Also, importantly, these samples – which provide all of the information to be discussed in this section – reflect only memory allocated and directly controlled by SLiM. Memory can be used by other factors too: SLiM's own executable code takes up memory, the operating system has memory overhead of various types, the C++ standard library makes allocations that SLiM has no way to measure, etc. However, in large simulations where memory usage is a concern, the memory allocated and directly controlled by SLiM is typically the large majority of the total memory usage, so this caveat should not prove limiting in practice.

So here we discover that in an average generation SLiM was using 0.56 GB of memory, but that at the end of the simulation the usage was 1.17 GB in the final generation. That suggests that the memory usage was increasing over the course of the simulation, which is typical since genetic diversity often builds up over time. Since the peak memory usage is typically the main concern, the final generation's statistics may usually be of the most interest. One might also wish to profile only the last 100 generations of a model, for example, in order to get averaged statistics that are not biased downward by the low memory usage toward the beginning of a run.

So far, so good; but these are only summary statistics. How does the memory usage by SLiM break down? What is all that memory actually being used for? A new section at the end of the profile report gives much more information:



SLiM memory usage (average / final generation)

```
0.73 KB / 0.73 KB : Chromosome object
   56 bytes / 56 bytes : mutation rate maps
   32 bytes / 32 bytes : recombination rate maps

0.73 MB / 0.73 MB : Genome objects (7992.01 / 8000)
   315.43 KB / 1.95 MB : external MutationRun* buffers
   17.98 KB / 18.00 KB : unused pool space
   0 bytes / 0 bytes : unused pool buffers

40 bytes / 40 bytes : GenomicElement objects (1.00 / 1)

160 bytes / 160 bytes : GenomicElementType objects (1.00 / 1)

0.88 MB / 0.89 MB : Individual objects (3996.00 / 4000)
   21.73 KB / 21.75 KB : unused pool space

352 bytes / 352 bytes : InteractionType objects (2.00 / 2)
   187.31 KB / 187.50 KB : k-d trees
   31.22 KB / 31.25 KB : position caches
   11.96 MB / 12.01 MB : sparse arrays

30.90 MB / 37.99 MB : Mutation objects (404963.41 / 497883)
   2.30 MB / 4.00 MB : refcount buffer
   15.04 MB / 42.01 MB : unused pool space

1.19 MB / 5.87 MB : MutationRun objects (17333.44 / 85518)
   134.08 MB / 316.42 MB : external MutationIndex buffers
   0 bytes / 0 bytes : nonneutral mutation caches
   1.31 MB / 8.54 MB : unused pool space
   153.97 MB / 472.74 MB : unused pool buffers

0.62 KB / 0.62 KB : MutationType objects (2.00 / 2)

2.34 KB / 2.34 KB : SLiMSim object
   220.07 MB / 290.31 MB : tree-sequence tables

0.73 KB / 0.73 KB : Subpopulation objects (1.00 / 1)
   15.61 KB / 15.62 KB : fitness caches
   31.22 KB / 31.25 KB : parent tables
   223 bytes / 224 bytes : spatial maps
   510.86 KB / 511.89 KB : spatial map display (SLiMgui only)

0 bytes / 0 bytes : Substitution objects (0.00 / 0)

Eidos:
   136.00 KB / 136.00 KB : EidosASTNode pool
   32.00 KB / 32.00 KB : EidosSymbolTable pool
   391.44 KB / 392.00 KB : EidosValue pool
```

Each line in this section gives average and final-generation usage statistics, separated by a slash, as suggested by the header. Usage is in bytes, KB, MB, GB, or potentially TB; since the units are mixed they must be noted carefully when comparing numbers. To make it easier to pick out the areas of highest impact, the usage statistics are color-coded in a similar way to the coloring of timing statistics earlier in the profile report; white is the lowest proportional usage (inconsequential in the big picture), and then shades of yellow, orange, and finally red reflect increasing proportions of total memory usage.

The report is broken down by the object responsible for the usage, sorted alphabetically; `Chromosome` comes first, `Substitution` last, with a small section on memory usage by Eidos at the end. The first line of each of these subsections gives the memory usage for the objects themselves; for the `Chromosome` section it gives the memory used by the one `Chromosome` object present in the simulation, for example. Subsequent lines give additional memory usage, by those objects, for particular purposes. For `Chromosome`, for example, the memory used by mutation rate maps and recombination rate maps is listed. This memory is not part of the `Chromosome` object itself; it is allocated *by* the `Chromosome` object. Each line thus stands on its own; the usage reported by lines under a given object type is not included in the first line. In other words, the hierarchy here is a conceptual hierarchy, not a breakdown of totals into sub-totals and sub-sub-totals. For most object types the number of objects allocated is also reported in parentheses; for example, there were `404963.41` mutation objects allocated in an average generation, and `497883` allocated in the final generation.

This breakdown shows that the majority of memory is taken up by `MutationIndex` buffers allocated by `MutationRun`; some are being used by currently allocated `MutationRun` objects, while others are attached to currently unused `MutationRun` objects in a pool of reusable mutation runs kept by SLiM for speed. These `MutationIndex` buffers are the way that SLiM keeps track of which mutations are present in each genome; they are like pointers to `Mutation` objects, but more compact since they are 32-bit indexes instead of 64-bit pointers. The `Mutation` objects themselves take up far less space, and are colored just a light yellow here; this is unsurprising and typical, for reasons discussed further in section 18.3.

Quite a substantial amount of memory is also taken up by the tree-sequence recording tables kept by SLiM, since tree-sequence recording is enabled in this model (see section 1.7). Tree-sequence recording can take up quite a bit of memory, but that memory usage can often be controlled (at the price of longer runtimes) by controlling the frequency of simplification of the tree-sequence tables; see the `simplificationRatio` parameter to `initializeTreeSeq()` in section 21.1). The model profiled here includes neutral mutations even though tree-sequence recording is enabled, which is usually not desirable or necessary, so it is paying a hefty price in memory usage (for illustration purposes).

Finally, a faint yellow tinge tells us that the sparse arrays kept by `InteractionType` are taking up a small but noticeable amount of memory. These keep track of the distances and interaction strengths between individuals; their size will scale with the number of individuals in a model, but will also be strongly affected by the maximum distance set for the spatial interactions in the model. The model profiled here uses very short maximum interaction distances, simulating a large landscape with very local interaction dynamics, which means that these data structures are quite small. In spatial models with broader spatial interaction kernels, these sparse arrays can take up much more space; indeed, in the worst case they can scale with the square of the number of individuals, and can account for the large majority of SLiM's memory usage. Keeping maximum interaction distances as small as possible is extremely important for SLiM's memory usage, and for its runtime too.

These memory usage statistics can, in some cases, provide a clear picture of how SLiM's memory usage could be reduced. This report, for example, could serve as a reminder that we probably want to turn off neutral mutations in the model, since tree-sequence recording would allow us to overlay them after simulation has completed (see section 16.2). If most of the memory usage of a simulation is in the `MutationIndex` buffers kept by `MutationRun`, that would similarly suggest that the simulation might benefit from the use of tree-sequence-recording. When that is not possible – when the mutations being simulated are non-neutral, for example – it may be necessary to reduce the scale of the model, in terms of population size, chromosome length, mutation rate, recombination rate, etc. Sections 5.5 and 18.3 have some further discussion of this.

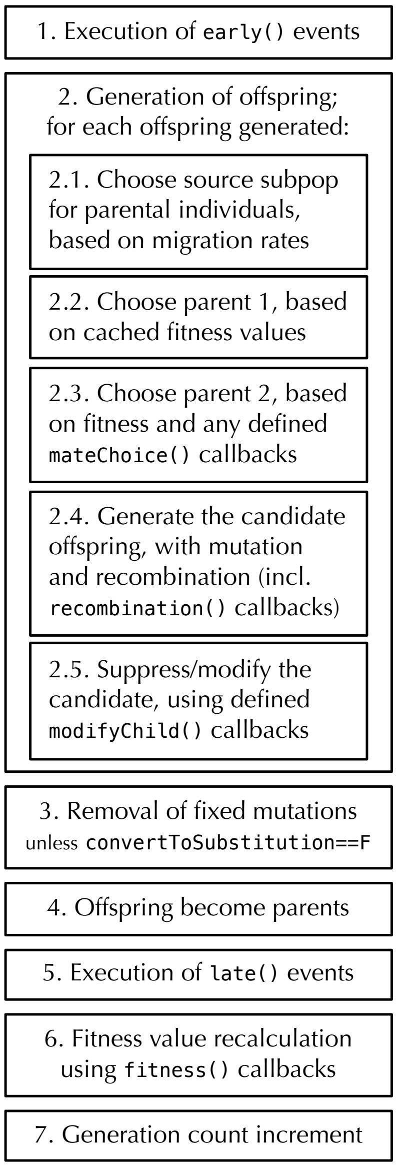
Part II: The SLiM Reference

19. SLiM architecture (WF models)

By default, SLiM uses a Wright-Fisher-type model of evolution, known in SLiM as a WF model (see section 1.6). This chapter will discuss the details of the generation cycle in WF models; chapter 20 provides the same type of discussion for nonWF models, a more advanced type of SLiM model.

Section 1.3 presented a summary of the life cycle followed by SLiM within each generation in WF models. The figure shown in that section is reproduced at right. In this chapter, we will examine each of these life cycle stages in more detail, in order to provide a more complete specification of the internal mechanics of SLiM.

The sequence of events within one generation in WF models.



1. Execution of early() events
2. Generation of offspring; for each offspring generated:
2.1. Choose source subpop for parental individuals, based on migration rates
2.2. Choose parent 1, based on cached fitness values
2.3. Choose parent 2, based on fitness and any defined mateChoice() callbacks
2.4. Generate the candidate offspring, with mutation and recombination (incl. recombination() callbacks)
2.5. Suppress/modify the candidate, using defined modifyChild() callbacks
3. Removal of fixed mutations unless convertToSubstitution==F
4. Offspring become parents
5. Execution of late() events
6. Fitness value recalculation using fitness() callbacks
7. Generation count increment

19.1 Step 1: Execution of `early()` Eidos events

The very first thing that happens in each generation is that the `active` property of all script blocks is reset to `-1` at the beginning of the generation, activating all script blocks for the remainder of the generation unless they are explicitly deactivated again. This is followed by the execution of `early()` Eidos events defined by the user, if any. Details on how to specify an Eidos event are given in section 22.1, with some further details in section 22.8 regarding their scheduling and the `active` property.

The salient point here is primarily that these events occur first in each generation, prior to the generation of offspring. If you wish to execute an Eidos event after offspring generation has completed, you should use a `late()` event; see section 19.5. Since the details of this step depend entirely on the script you write, there is little more to say about this step.

19.2 Step 2: Generation of offspring

This is the most complex step in SLiM's architecture, and it is broken down into five sub-steps that are executed for each offspring generated, as shown in the figure at right. Processes involved in the generation of offspring include migration, mate choice, mutation, recombination, and the actual production of offspring individuals.

19.2.1 The order of offspring generation

For each offspring generated, there are generally several decisions to be made: (1) is the offspring local, or if not, from which other subpopulation are its parents drawn, (2) is it male or female (in sexual simulations), and (3) is it produced by cloning, selfing, or biparental mating? In SLiM, the sex ratio specified for a subpopulation is deterministic; SLiM will produce that exact sex ratio in each generation (so as to avoid the possibility of extinction due to the chance production of a single-sex child generation). The other decisions are made stochastically; migration rates, selfing rates, and cloning rates are all probabilities, not deterministic ratios, and you can think of SLiM as rolling the dice to make these decisions for each offspring individual. This means that the sex ratio of a subpopulation does not fluctuate over time, but the fraction of offspring that are migrants, or clones, or selfed, will vary stochastically around the specified rates.

The order in which offspring are generated, with respect to these decisions, depends upon the details of your simulation. In the base case, SLiM produces offspring in deterministic tranches; for example, migrants before locals, and within that, males before females, and within *that*, cloned before selfed before biparental. The specifics of this ordering are not guaranteed; the main point is that you should not rely on the order of offspring being random. In particular, you should randomly select genomes when doing things like inserting new mutations, to overcome the possibility of order-dependency and bias (as shown in the recipe in section 10.1). If `mateChoice()`, `modifyChild()`, or `recombination()` callbacks are defined, SLiM switches its behavior to generate offspring in a randomized order, rather than in these deterministic tranches. This presents mating and offspring decisions to those callbacks in a random order, so that bias is not inadvertently introduced by callbacks.

SLiM is fundamentally a model of juvenile migration, not migration at the adult stage. This has several consequences for these decisions that are made for each offspring. First of all, if the offspring is a migrant produced biparentally, it should be noted that both parents will be drawn from the same source subpopulation; matings between parents in different subpopulations never occur in SLiM, since adults do not migrate. Second, it should be noted that the parental source subpopulation is "in charge" of most of the decisions made regarding the offspring, since the offspring is produced within that source subpopulation by the mating of parentals in that subpopulation. In particular, the source subpopulation determines the cloning rate and selfing rate, as well as the `mateChoice()`, `modifyChild()`, and `recombination()` callbacks used. The only exception is sex ratio; the sex ratio of the destination subpopulation governs the ratio of males to females produced in that subpopulation, regardless of the sex ratios specified by the various source subpopulations contributing migrants.

19.2.2 Mate choice

Once the decisions outlined in the previous section have been made for a given offspring (parental subpopulation, sex, clonal/selfed/biparental), the next step in offspring generation is choosing the parent(s) for the offspring. The precise way in which this is done depends upon the type of offspring being produced:

(1) If the offspring is to be clonal, a single parent is drawn randomly, according to probabilities proportional to fitness, from the source subpopulation. Any `mateChoice()` callbacks defined are not called; there is presently no way to influence the choice of clonal parents except by modifying fitness values with a `fitness()` callback. Offspring generation proceeds along a different path in this case, introducing mutations as usual (see below) but without recombination.

(2) If the offspring is to be selfed, a single parent is drawn according to fitness, as with cloning. That parent is then considered to be a forced choice for the second parent; `mateChoice()` callbacks are not used. Offspring generation proceeds thereafter as with biparental mating.

(3) If the offspring is to be the result of biparental mating, a first parent is drawn according to fitness; in sexual simulations the first parent will always be female, since SLiM models female choice. If no `mateChoice()` callbacks are defined, a second parent is then drawn according to fitness – in sexual simulations, always a male. If `mateChoice()` callbacks are defined, on the other hand, those callbacks will be called to determine mating weights for all eligible parents given the chosen first parent, as detailed in section 22.3 and 17.6, and a second parent will then be drawn according to those mating weights. If the `mateChoice()` callbacks completely reject the first parent, offspring generation will go back to almost the beginning of the process, but the source subpopulation will remain unchanged, as will the sex of the offspring to be produced (but the cloned/selfed/biparental decision, and the choice of the first parent, will be made over from scratch).

19.2.3 Mutation and recombination

Once a parent or parents have been successfully selected, as detailed in the previous subsection, a candidate offspring is generated from the chosen parent(s). As the first step in this process, the mutations to be introduced into each of the two offspring genomes are generated. The number of mutations is determined by the current mutation rate, using a draw from the appropriate Poisson distribution. The particular mutations are then generated one by one, each with a position drawn at random from within all of the defined genomic elements in the chromosome. Given that position, the identity of the genomic element and thus the controlling genomic element type is determined. Using the list of mutation types and associated probabilities for the genomic element type, a particular mutation type is chosen probabilistically. Finally, a selection coefficient is drawn from the chosen mutation type (see section 21.8), and a new `Mutation` object is constructed with the selection coefficient. In this manner, all of the new mutations to be introduced into each of the two offspring genomes are generated.

If the offspring is to be produced clonally, what follows is then relatively simple: conceptually, the parental genomes are replicated exactly in the offspring, and then the mutations are interleaved into the offspring genomes at their particular positions.

If the offspring is to be produced by selfing or biparentally (which are identical at this stage of the process), recombination is also involved, making the process somewhat more complex. The first offspring genome is produced via recombination between the two genomes of the first parent, and the second offspring genome is produced via recombination between the two genomes of the second parent (mimicking the process of meiosis to produce haploid gametes that merge to form a fertilized egg). For each offspring genome, the number of recombination breakpoints is drawn from a Poisson distribution based upon the overall recombination rate (computed internally by SLiM). The position of each breakpoint is then drawn, based upon the recombination ranges and rates set on the chromosome. If a non-zero probability of gene conversion is set, and a random draw indicates that gene conversion actually occurs for a given breakpoint, an additional breakpoint (above and beyond the drawn number of breakpoints) will be added following the converted breakpoint, with a positional offset drawn from a geometric distribution satisfying the requested average gene conversion length. Note that occasionally this additional breakpoint will fall *after* another drawn breakpoint position; this will result in a gene conversion stretch that is shorter than the drawn gene conversion length, since the first breakpoint position will end gene conversion. If `recombination()` callbacks are defined, they are called at this point to allow them to modify the crossover points and the gene conversion stand and end points. Finally, given the two genomes from the parent, the list of recombination breakpoints, and the set of mutations to be introduced, SLiM then weaves together the final genome of the offspring, alternating between the two parental genomes as dictated by the recombination breakpoints, and introducing mutations at the chosen positions.

By default, SLiM allows multiple mutations to exist at the same site in a single individual – "stacked" mutations, as we call them. This behavior is often desirable, but sometimes it is useful to prevent stacked mutations of a given mutation type. The stacking policy of a given mutation type can be changed using `MutationType`'s `mutationStackPolicy` and `mutationStackGroup` properties, as documented in section 21.9.1.

19.2.4 Child modification

Once the two genomes of the candidate offspring have been generated, as described in the previous section, child modification by `modifyChild()` callbacks (described in sections 21.4 and 21.8) occurs, if any callbacks are active. These callbacks are called regardless of whether the offspring was the product of cloning, selfing, or biparental mating; all types of children may be modified.

These callbacks may modify the candidate offspring in any way desired. For our purposes here, the only question arises with the possibility that a `modifyChild()` callback will suppress the candidate offspring altogether, rather than just modifying it. This can be thought of as representing juvenile mortality, if you wish; it could also represent postmating reproductive isolation, such as infertility or developmental inviability. In some cases, suppression of a candidate offspring can also be thought of as representing a type of mate choice.

When a candidate offspring is suppressed, generation of the offspring goes back almost to the beginning of the process, as with rejection of the first parent by a `mateChoice()` callback. In fact, in this case the process goes back even further; a new source subpopulation for the offspring is chosen, in addition to re-making the cloned/selfed/biparental decision and re-choosing the parents. The only aspect of the offspring generation that is not re-decided in this case is the sex of the planned offspring individual; that remains fixed since the sex ratio is deterministic, not stochastic. Note that this means that if a `modifyChild()` callback suppresses a candidate offspring, the next time it is called the new candidate will be the same sex as the previously suppressed candidate. Because of this, it is not possible for a `modifyChild()` callback to influence the sex ratio of a subpopulation; attempting to do so will produce an infinite loop.

19.2.5 Child generation

Once a candidate offspring has been generated and modified, and was not suppressed by a `modifyChild()` callback, it is added to the target subpopulation. Note that the newly added child will not be visible as a member of the subpopulation until the point in the lifecycle when the child generation becomes the parental generation (see section 19.4). This prevents order-dependencies in which the first children generated might otherwise influence the remainder of the child generation process.

19.3 Step 3: Removal of fixed mutations

After all offspring have been generated for all subpopulations, SLiM performs bookkeeping regarding the mutations in the simulation. In particular, it scans through every genome in every individual in every subpopulation, and tallies up how many times each of the mutations in the simulation is actually present in the child generation.

The results from this scan are used to clean house. If a mutation is no longer referenced by any genome in the simulation, that mutation has been lost (whether due to selection or drift), and SLiM forgets about it. If, on the other hand, a mutation is now contained by *every* genome in the simulation, that mutation has fixed. In this case, SLiM normally creates a new `Substitution` object as a placeholder, to record the details of the fixed mutation, and then removes the mutation from the simulation. This is essentially an optimization for efficiency; if fixed mutations were not removed, a long-running simulation would accumulate ever more mutations needing to be tracked. In general the substitution is harmless; a fixed mutation cannot generally decrease in frequency, and generally no longer influences fitness (since it is possessed by all individuals, and thus has an identical effect on the fitness of all individuals).

However, there are specific circumstances in which the removal of fixed mutations is not desirable. In particular, if the fixed mutation would continue exerting a varying effect on fitness among individuals (because of epistasis, for example), the substitution of the mutation would result in incorrect fitness values. Also, if the script for a simulation intends to remove the mutation from some genomes later in the simulation run (perhaps simulating a back-mutation) then it would be desirable to prevent the substitution of the mutation. To accommodate these possibilities, the `convertToSubstitution` property of a mutation type can be set to `F` to suppress substitution of mutations of that type; see section 21.9.1.

19.4 Step 4: Offspring become parents

As mentioned in section 19.2.5, newly generated offspring are kept by SLiM as members of a child generation that is not visible to the model mechanics (or to your Eidos scripts), to avoid order-dependencies and other confusion. After fixed mutations have been removed, as described in the previous section, the child generation becomes the new parental generation, and the old parental generation is discarded.

19.5 Step 5: Execution of `late()` Eidos events

After the child generation is promoted to the parental generation, the next step is to execute `late()` Eidos events defined by the user, if any. Details on how to specify an Eidos event are given in section 22.1, with some further details in section 22.8 regarding their scheduling and the `active` property. Eidos `late()` events are most often used when output is being generated (since you typically want to output the state of the simulation at the end of a generation, not at the beginning), and when adding or removing mutations (since you want those changes to be reflected in the fitness values calculated for individuals, prior to the next offspring generation step). Changing of selection or dominance coefficients should also typically be done in a `late()` event, for the same reason. See sections 4.2.1, 10.1, and 10.6.1 for discussion and examples.

19.6 Step 6: Fitness value recalculation

After the child generation is promoted to the parental generation, the next step is to compute fitness values for the new adult individuals, including the effects of any `fitness()` callbacks. Fitness values computed at the end of one generation are actually used during mating in the following generation; this is something to keep in mind if you are designing `fitness()` callbacks that you want to be active only across a specific generation range. The reason SLiM does this has to do mostly with running in SLiMgui; it is desirable that SLiMgui should show newly-calculated fitness values for the new parental generation when single-stepping through generations. If fitness values were not calculated until the beginning of the next generation, they would not yet be available for display.

If `fitness()` callbacks are not active for a given subpopulation, calculating the fitness of an individual is relatively straightforward. SLiM uses a model of multiplicative fitness between sites. An initial relative fitness *w* of `1.0` is assumed for the individual (unless `fitnessScaling` values have been set; in fact, the initial fitness *w* is the product of the individual's `fitnessScaling` property and its subpopulation's `fitnessScaling` property, but these properties are `1.0` by default). Then, each mutation possessed by the individual is evaluated as to whether it is present in just one of the individual's genomes (i.e. is heterozygous) or is present in both genomes (i.e. is homozygous). If a mutation is homozygous, the individual's relative fitness is updated as:

$$w = w * (1.0 + \text{selectionCoefficient}),$$

whereas if the mutation is heterozygous, the relative fitness is updated as:

$$w = w * (1.0 + \text{dominanceCoeff} * \text{selectionCoeff}).$$

where the dominance coefficient of the mutation is defined by the mutation's mutation type, in the default case of simulating autosomes. For simulations of the X chromosome, the mutation type's dominance coefficient is used for heterozygous XX females, whereas XY males that are "heterozygous" because they possess the mutation on their lone X chromosome use a global dominance coefficient (see `initializeSex()`, section 21.1, and the `dominanceCoeffX` property of `SLiMSim`, section 21.12.1). Simulations of the Y chromosome do not use a dominance coefficient at all; the first of the two formulas above is used. If the new relative fitness is zero or less, the mutation just evaluated was lethal, and so the final relative fitness of the individual is `0.0`. Otherwise, SLiM proceeds with evaluating the next mutation, until all mutations have been evaluated to produce a final relative fitness value.

If `fitness()` callbacks are defined (as described in section 22.2), this procedure is modified slightly. In this case, the multiplicative effect on relative fitness that would be produced by a given mutation is calculated, exactly as above, but instead of simply multiplying *w* by that fitness effect, SLiM calls out to `fitness()` callbacks to allow them to modify the relative fitness value. After callbacks, *w* is multiplied by the final fitness effect for the mutation. The `fitness()` callback calculates the relative fitness of the mutation in the individual, whether the mutation is heterozygous or homozygous; if you wish the calculated fitness value to be different in those two cases, then the `fitness()` callback needs to explicitly take the heterozygosity of the mutation into account (which is part of the information provided to the callback by SLiM, so doing so is not difficult; see section 22.2).

In SLiM version 2.3 and later, it is possible to define *global* `fitness()` callbacks, which are applied exactly once to every individual without reference to a focal mutation or a particular mutation type (see section 22.2). The fitness values returned by global `fitness()` callbacks are multiplied in to the fitness value previously computed for the individual, as:

w = *w* * relativeFitness.

The fitness effects of global `fitness()` callbacks thus combine multiplicatively with all of the fitness effects of mutations, and multiple global `fitness()` callbacks may be defined. Unlike other types of callbacks, the order in which global `fitness()` callbacks are called is formally undefined, both relative to other global `fitness()` callbacks and relative to ordinary (i.e., non-global) `fitness()` callbacks. Also note that global fitness callbacks might not be called at all for a given individual if that individual's fitness has already been determined, by previous callbacks or fitness effects, to be equal to zero. Models should therefore be extremely cautious in making any assumptions whatsoever regarding the timing or order in which global `fitness()` callbacks will be executed, or whether they will be executed at all; global `fitness()` callbacks that have external side effects, such as changing the `active` property of script blocks or defining Eidos constants, are not recommended.

In SLiM 3.0 and later, the `fitnessScaling` property may be set on the subpopulation or the individual (or both) to multiplicatively influence individual fitness values, as mentioned above. This is often a more efficient and simpler alternative to defining a global `fitness()` callback.

One caveat is that fitness calculations are done sequentially for all of the individuals in each subpopulation, rather than being done in a random order. This means that `fitness()` callbacks should be written in such a way as to make each fitness computation independent of all others, and independent of the order in which they are done. A `fitness()` callback that produces a different result the first time it is run in a generation compared to subsequent times, for example, would introduce bias and order-dependency into a model, particularly since the order of genomes in each subpopulation is not necessarily random (see section 19.2.1).

19.7 Step 7: Generation count increment

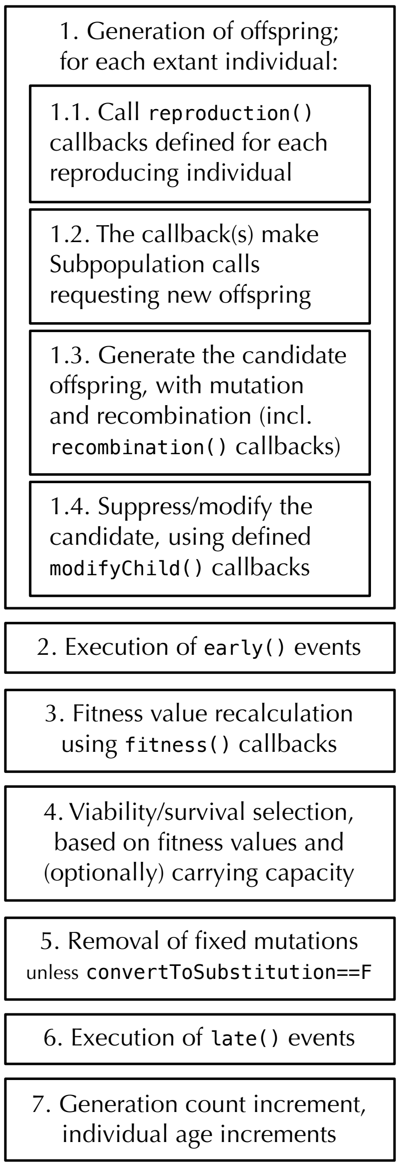
The final step in each generation is that the generation count is incremented. SLiM then checks whether the simulation is over; if there are no events or callbacks scheduled to execute in the new generation or any subsequent generation (not counting events and callbacks with no specified end generation), the simulation is deemed to be over, and execution halts.

20. SLiM architecture (nonWF models)

By default, SLiM uses a Wright-Fisher-type model of evolution, known in SLiM as a WF model – but an alternative non-Wright-Fisher, or nonWF, model type may be chosen instead (see section 1.6 and chapter 15). This chapter will discuss the details of the generation cycle in such models. Chapter 19 provides such discussion for WF models; to avoid a lot of duplicated verbiage, this chapter will assume familiarity with the WF generation cycle as described in chapter 19, and will make reference to that chapter rather than spelling out every detail a second time.

The figure shown at right is a summary of the life cycle followed by SLiM within each generation in nonWF models. In this chapter, we will examine each of these life cycle stages in more detail, in order to provide a more complete specification of the internal mechanics of SLiM.

The sequence of events within one generation in nonWF models.


1. Generation of offspring; for each extant individual:
1.1. Call `reproduction()` callbacks defined for each reproducing individual
1.2. The callback(s) make Subpopulation calls requesting new offspring
1.3. Generate the candidate offspring, with mutation and recombination (incl. `recombination()` callbacks)
1.4. Suppress/modify the candidate, using defined `modifyChild()` callbacks
2. Execution of `early()` events
3. Fitness value recalculation using `fitness()` callbacks
4. Viability/survival selection, based on fitness values and (optionally) carrying capacity
5. Removal of fixed mutations unless `convertToSubstitution==F`
6. Execution of `late()` events
7. Generation count increment, individual age increments

20.1 Step 1: Generation of offspring

In nonWF models, the first thing to happen each generation is the generation of new offspring. (OK – technically, as in WF models, this is preceded by resetting the `active` properties of all script blocks; see section 19.1). This is the most complex step in SLiM's architecture, and in nonWF models it is broken down into four sub-steps that are executed for each offspring generated, as shown at right. Processes involved in the generation of offspring include mate choice, mutation, recombination, and the actual production of offspring individuals. (In WF models, migration is also effected during offspring generation, but this is not the case in nonWF models.)

20.1.1 The order of offspring generation

For each offspring generated, there are generally several decisions to be made: (1) what are its parents, (2) is it male or female (in sexual simulations), and (3) is it produced by cloning, selfing, or biparental mating? In WF models, these decisions are made by SLiM's core engine, as described in section 19.2.1, based upon parameters such as the sex ratio, cloning rate, and selfing rate, as well as upon individual fitness values and the results from `mateChoice()` callbacks. In nonWF models, in contrast, all of these decisions are made by the model's script: `reproduction()` callbacks are called once for each individual in the model, to request that each individual generates its own offspring to be added to the population.

The order in which individuals are asked to generate their offspring is always random in nonWF models, across the entire population, to try to prevent order-dependencies from biasing offspring generation. In addition to this, however, it is important to design your `reproduction()` callbacks to be independent; in general, the reproductive behavior of each individual should probably be independent of the reproductive behavior of every other individual, so whether `A` is asked to reproduce before `B`, or `B` before `A`, does not bias the outcome of the model. There are certainly cases where you might violate this principle; in a model of monogamous mating, for example, the first female asked to reproduce might be able to claim her choice of males, whereas the last female asked to reproduce might have little or no choice since most males would already be claimed. Sometimes such asymmetries are acceptable or even desirable; sometimes, however, they would constitute a bug. So the message of this subsection is primarily: think carefully about the order of offspring generation, and about the independence of each reproductive event (or the lack thereof), and make sure your models does what you really want it to.

20.1.2 Individual-based reproduction with `reproduction()` callbacks

As mentioned above, `reproduction()` callbacks are called for each individual in the model. The task of each callback is to generate the offspring from one focal individual. In sexual models, perhaps females would generate offspring and males would not (or perhaps the opposite, if males are the choosy sex in the biological system being modeled). In monogamous-mating models, a single mate might be chosen and then a litter of offspring generated through crosses with that mate; in a non-monogamous model each offspring generated might be with a different mate. Some offspring might be generated via cloning or selfing, rather than biparental mating. The sex of offspring in sexual models might be equally likely to be male or female, or there might be some sex-ratio bias. Most importantly, in nonWF models all of these decisions can depend upon the genetics and other state of each individual, rather than being dictated by overall parameters as in WF models.

Regardless of how a given model makes these decisions, it always expresses them to SLiM in one way: by making method calls on `Subpopulation` objects, requesting the addition of new offspring. There are four methods that can be called: `addCrossed()` to add an offspring resulting from a biparental cross, `addSelfed()` to add an offspring resulting from selfing (i.e., sexual self-fertilization in a hermaphroditic individual), `addCloned()` to add an offspring resulting from clonal reproduction, or `addEmpty()` to an offspring with no parents and no empty genomes (presumably to be filled in some special way by script, subsequently). Each such method call made sets off the chain of events described in the following subsections: mutation and recombination, child modification, and child generation.

20.1.3 Mutation and recombination

Mutation and recombination occur in nonWF models exactly as they do in WF models; see section 19.2.3 for details.

20.1.4 Child modification

Child modification, via `modifyChild()` callbacks, occurs in nonWF models largely as it does in WF models; see section 19.2.4 for details. The important difference is that whereas WF models have a target subpopulation size to reach, and thus must keep generating offspring until that target is reached, the same is not true of nonWF models. In nonWF models, therefore, if a `modifyChild()` callback returns `F` to indicate that a given offspring should not be generated (due to postmating reproductive isolation or genetic incompatibility, for example), that is the end of it. That offspring will simply not be generated; there will be one fewer offspring individual, in the end, than there would have been if the `modifyChild()` callback had returned `T`. In this case, the `Subpopulation` method call that initiated offspring generation, such `addCrossed()`, will return `NULL` to its caller. This is generally desirable; see section 22.7 for further discussion of how this behavior interacts with `reproduction()` callbacks.

20.1.5 Child generation

Once a candidate offspring has been generated and modified, and was not suppressed by a `modifyChild()` callback, it is queued for addition to the target subpopulation. Note that the newly added child will not be visible as a member of the subpopulation until the end of offspring generation. This prevents newly generated offspring from being chosen as mates, or otherwise influencing the remainder of the child generation process.

20.2 Step 2: Execution of `early()` Eidos events

Offspring is followed by the execution of `early()` Eidos events defined by the user, if any. The mechanics of this are the same as in WF models, but the semantics of `early()` versus `late()` events are actually reversed in nonWF models, in some ways.

In WF models, `early()` events occur just before offspring generation and `late()` events happen just after; in nonWF models this positioning is reversed, because offspring generation has been moved earlier in the generation cycle. Similarly, in WF models `late()` events are usually the best place to add new mutations, because the next stage is fitness evaluation, which immediately incorporates the fitness effects of the new mutations; but in nonWF models `early()` events are usually the best place to add new mutations, for the same reason.

In WF models, `late()` events are generally the best place to put output events so that they reflect the final state at the end of a generation; in nonWF models, however, output can make sense in either an `early()` or a `late()` event, depending upon whether you want to see the state of the population before or after viability selection. However, reading in a previously written output file, or otherwise setting up new population state, is generally best done in an `early()` event in nonWF models so that fitness values are recalculated immediately after the change (just as with adding new mutations). So if you call `outputFull()` with the intention of reading the output back in with `readFromPopulationFile()` later, you will probably want to do the output in an `early()` event so that you can, correspondingly, do the read in an `early()` event as well without skipping or doubling any generation cycle stages.

For those who are curious: the reason for this reordering of the generation cycle in nonWF models is the addition of the viability/survival generation cycle stage, which does not exist in WF models. It is desirable to have an opportunity for scripted events between offspring generation and selection, and then between selection and the next offspring generation stage. It is also desirable for selection to happen *after* offspring generation in the cycle, so that the population state at the end of each generation (as displayed in SLiMgui, for example) is after selection has occurred. These constraints, taken together, dictate the order of the generation cycle in nonWF models.

20.3 Step 3: Fitness value recalculation

After the execution of `early()` events, the next stage in nonWF models is to compute fitness values for all individuals, including the effects of any `fitness()` callbacks. The mechanics of this are exactly the same in nonWF models as in WF models; see the extensive discussion in section 19.6.

However, because of the reordering of the generation cycle, the semantics of fitness evaluation in nonWF models are a bit different. In WF models, as section 19.6 explains, the fitness values calculated in generation `T` are actually used, to influence mating, in generation `T+1`. In nonWF models, however, fitness values calculated in generation `T` are then used immediately, in generation `T`, to influence survival (see the next subsection). This oddity of WF models is therefore not present in nonWF models, making them a bit conceptually simpler.

The actual meaning of individual fitness values is also different between WF and nonWF models; see the next section for discussion.

20.4 Step 4: Viability/survival selection

After fitness values have been recalculated for all individuals, viability selection then occurs immediately. In WF models, viability selection does not exist (or you could consider new offspring to have a survival rate of 100%, and the parental generation to have a survival rate of 0%, if you like). In nonWF models, in contrast, viability selection is the primary way in which differential fitness is expressed; individual fitness values influence survival, not mating success.

Viability selection in nonWF models is mechanistically simple. For a given individual, a fitness of `0.0` or less results in certain death; that individual is immediately removed from its subpopulation. A fitness of `1.0` or greater results in certain survival; that individual remains in its subpopulation, and will live into the next generation cycle. A fitness greater than `0.0` and less than `1.0` is interpreted as a survival probability; SLiM will do a random draw to determine whether the individual survives or not.

This change in the way individual fitness is used has large consequences. First of all, it means that in nonWF models fitness is *absolute* fitness, whereas in WF models fitness is *relative* fitness. Second, it means that in nonWF models selection is generally *hard* selection, reducing the size of the population proportionate to mean population fitness, whereas in WF models it is generally *soft* selection, changing the relative success of particular genes but not changing the size of the population. Third, it means that in nonWF models the population is not automatically regulated – both extinction and unbounded exponential growth are very real possibilities – whereas in WF models SLiM automatically regulates the population size. These three observations are all really different ways of looking at the same basic fact.

Because of this shift, nonWF models need to treat individual fitness differently than WF models. For one thing, there is generally a need to introduce some sort of density-dependent fitness, in a global `fitness()` callback, that prevents exponential growth by decreasing individual fitness as the population size gets larger. Second, there may be a need to rethink how beneficial mutations work, since increasing the fitness of an individual above `1.0` has no effect in nonWF models (since guaranteed survival is as good as it gets); it may be desirable to have a baseline fitness, for individuals possessing empty genomes, of less than `1.0` so that beneficial mutations can increase the probability of survival above that baseline. This would also be achieved with a global `fitness()` callback (perhaps in conjunction with density-dependence). All of this is entirely up to the model's script.

Finally, it is worth noting that it is certainly to have genetics and other individual state influence mating success and/or fecundity in nonWF models, as in WF models. In nonWF models that is done by influencing the dynamics in the offspring generation stage in script, however; it is not an automatic consequence of the fitness values calculated by SLiM.

20.5 Step 5: Removal of fixed mutations

After viability selection, SLiM tallies mutation frequencies and removes fixed and lost mutations. The mechanics of this are essentially the same as in WF models; see section 19.3.

However, there is one important difference here between WF and nonWF models. In WF models, fixed mutations can generally be removed because they no longer influence evolutionary dynamics, as a consequence of fitness values being *relative* fitness. If every individual in the population is fixed for a given mutation, then that mutation has no effect on relative fitness, regardless of what its selection coefficient might be; the only exceptions are cases where the fitness effect of the mutation varies from individual to individual, such as when epistatic interactions with other segregating mutations are present. In WF models, the `convertToSubstitution` property of mutation types therefore defaults to `T`, allowing SLiM to remove fixed mutations by default; when that is not desirable, models need to set `convertToSubstitution` to `F` to prevent that automatic removal.

In nonWF models, in contrast, the `convertToSubstitution` property defaults to `F`, because in general it is not safe for SLiM to remove fixed mutations; models need to set it to `T` to allow automatic removal. Generally, in nonWF models automatic removal of fixed mutations only makes sense if several conditions are met: (1) the mutation is neutral, (2) the mutation has no direct non-neutral effects due to any `fitness()` callback, and (3) the mutation has no indirect non-neutral effects on the model through epistasis, mate choice, fecundity, or any other such influences on the model. If these conditions are met – as is commonly the case for simple neutral background mutations – it is very important to set `convertToSubstitution` to `T`; the effect on SLiM's performance can be very large!

20.6 Step 6: Execution of `late()` Eidos events

Once fixed mutations have been removed, the next step is to execute any defined and active `late()` events. This works identically to WF models (see section 19.5). The only important difference is the way in which the semantics and common uses of `early()` and `late()` events differ between WF and nonWF models, as discussed in section 20.2.

20.7 Step 7: Generation count increment

As in WF models, the last stage of the generation cycle is the incrementing of the generation count and the check for the simulation being finished (see section 19.7). In nonWF models, the age of all surviving individuals is also incremented by one during this stage.

21. SLiM classes

This chapter presents reference documentation for all of the Eidos classes built into SLiM. It assumes an understanding of the syntax of type-specifiers and method signatures, including the use of optional arguments and default values. It also assumes an understanding of how classes are used in Eidos, including how properties are accessed and how methods are called. Part I of this manual attempts to introduce those topics to some degree, but see the Eidos manual for more extensive discussion and documentation of these fundamental language features.

A caveat to keep in mind throughout this section is that SLiM 2 and later (unlike SLiM 1.8 and earlier) generally uses zero-based values; a chromosome might start at index `0` and go to index `99999`, for example. Eidos and SLiMgui present this zero-based worldview as well.

21.1 Simulation initialization: `initialize()` callbacks

Before a SLiM simulation can be run, the various classes underlying the simulation need to be set up with an initial configuration. In SLiM 1.8 and earlier, this was done by means of `#` directives in the simulation's input file. In SLiM 2 and later, simulation parameters are instead configured using Eidos.

Configuration in Eidos is done in *`initialize()` callbacks* that run prior to the beginning of simulation execution. Eidos callbacks are discussed more broadly in chapter 22, but for our present purposes, the idea is very simple. In your input file, you can simply write something like this:

```
initialize() { ... }
```

The `initialize()` specifies that the script block is to be executed as an `initialize()` callback before the simulation starts. The script between the braces `{}` would set up various aspects of the simulation by calling *initialization functions*. These are SLiM functions that may be called only in an `initialize()` callback, and their names begin with `initialize` to mark them clearly as such. You may also use other Eidos functionality, of course; for example, you might automate generating a large number of subpopulations with complex migration patterns by using a `for` loop.

One thing worth mentioning is that in the context of an `initialize()` callback, the `sim` global for the simulation itself is not defined. This is because the state of the simulation is not yet constructed fully, and accessing partially constructed state would not be safe.

Without further ado, then, here are the initialization functions provided by SLiM:

`(void)initializeGeneConversion(numeric$ conversionFraction, numeric$ meanLength)`

Configure the likelihood and behavior of gene conversion events. The probability of gene conversion occurring for any one recombination event is given by `conversionFraction`, and the mean of the geometric distribution from which the length of the gene conversion stretch will be drawn is specified by `meanLength` (specified in base positions). Note that chromosome positions with a recombination rate of exactly `0.5` will not be candidates for gene conversion, as it is assumed that they represent junction points between discrete chromosomes.

```
(void)initializeGenomicElement(io<GenomicElementType>$ genomicElementType,
    integer$ start, integer$ end)
```

Add a genomic element to the chromosome at initialization time. The `start` and `end` parameters give the first and last base positions to be spanned by the new genomic element. The new element based upon the genomic element type identified by `genomicElementType`, which can be either an `integer`, representing the ID of the desired element type, or an `object` of type `GenomicElementType`, specified directly.

```
(object<GenomicElementType>$)initializeGenomicElementType(is$ id,
    io<MutationType> mutationTypes, numeric proportions)
```

Add a genomic element type at initialization time. The `id` must not already be used for any genomic element type in the simulation. The `mutationTypes` vector identifies the mutation types used by the genomic element, and the `proportions` vector should be of equal length, specifying the relative proportion of mutations that will be draw from the corresponding mutation type (proportions do not need to add up to one; they are interpreted relatively). The `id` parameter may be either an `integer` giving the ID of the new genomic element type, or a `string` giving the name of the new genomic element type (such as `"g5"` to specify an ID of 5). The `mutationTypes` parameter may be either an `integer` vector representing the IDs of the desired mutation types, or an `object` vector of `MutationType` elements specified directly. The global symbol for the new genomic element type is immediately available; the return value also provides the new object.

```
(object<InteractionType>$)initializeInteractionType(is$ id, string$ spatiality,
    [logical$ reciprocal = F], [numeric$ maxDistance = INF],
    [string$ sexSegregation = "**"])
```

Add an interaction type at initialization time. The `id` must not already be used for any interaction type in the simulation. The `id` parameter may be either an `integer` giving the ID of the new interaction type, or a `string` giving the name of the new interaction type (such as `"i5"` to specify an ID of 5).

The `spatiality` may be `""`, for non-spatial interactions (i.e., interactions that do not depend upon the distance between individuals); `"x"`, `"y"`, or `"z"` for one-dimensional interactions; `"xy"`, `"xz"`, or `"yz"` for two-dimensional interactions; or `"xyz"` for three-dimensional interactions. The dimensions referenced by spatiality must have been previously defined as spatial dimensions with `initializeSLiMOptions()`; if the simulation has dimensionality `"xy"`, for example, then interactions in the simulation may have spatiality `""`, `"x"`, `"y"`, or `"xy"`, but may not reference spatial dimension *z* and thus may not have spatiality `"xz"`, `"yz"`, or `"xyz"`. If no spatial dimensions have been configured, only non-spatial interactions may be defined.

The `reciprocal` flag may be `T`, in which case the interaction is guaranteed by the user to be *reciprocal*: whatever the interaction strength is for individual B upon individual A, it will be equal (in magnitude and sign) for A upon B. This allows the `InteractionType` to reduce the amount of computation necessary by up to a factor of two. If `reciprocal` is `F`, the interaction is not guaranteed to be reciprocal and each interaction will be computed independently. The built-in interaction formulas are all reciprocal, but if you implement an `interaction()` callback (see section 22.6), you must consider whether the callback you have implemented preserves reciprocality or not. For this reason, the default is `reciprocal=F`, so that bugs are not inadvertently introduced by an invalid assumption of reciprocality. See below for a note regarding reciprocality in sexual simulations when using the `sexSegregation` flag.

Note that even if an interaction is reciprocal, it may occasionally be slightly faster for `reciprocal` to be set to `F`. This is most likely when the amount of computation per interaction is very small (particularly if no `interaction()` callbacks are involved), and when it is unlikely that the reciprocal of a queried interaction will also be queried. Even in such cases, however, the slowdown for `reciprocal=T` should be fairly small. In most usage cases, setting `reciprocal` to `T` (when the interaction is in fact reciprocal) will result in at least equal performance, if not better; with a very slow `interaction()` callback, the performance can be as much as double, making it generally worthwhile to use `reciprocal=T` when possible. However, for maximal performance one might wish to time and compare runs with reciprocality enabled and disabled (using the same random number seed).

The `maxDistance` parameter supplies the maximum distance over which interactions of this type will be evaluated; at greater distances, the interaction strength is considered to be zero (for efficiency). The default value of `maxDistance`, `INF` (positive infinity), indicates that there is no maximum interaction distance; note that this can make some interaction queries much less efficient, and is therefore not recommended. In SLiM 3.1 and later, a warning will be issued if a spatial interaction type is defined with no maximum distance to encourage a maximum distance to be defined.

The `sexSegregation` parameter governs the applicability of the interaction to each sex, in sexual simulations. It does not affect distance calculations in any way; it only modifies the way in which interaction strengths are calculated. The default, `"**"`, implies that the interaction is felt by both sexes (the first character of the `string` value) and is exerted by both sexes (the second character of the `string` value). Either or both characters may be `M` or `F` instead; for example, `"MM"` would indicate a male-male interaction, such as male-male competition, whereas `"FM"` would indicate an interaction influencing only females that is influenced only by males, such as male mating displays that influence female attraction. This parameter may be set only to `"**"` unless sex has been enabled with `initializeSex()`. Note that a value of `sexSegregation` other than `"**"` may imply some degree of non-reciprocality, but it is not necessary to specify `reciprocal` to be `F` for this reason; SLiM will take the sex-segregation of the interaction into account for you. The value of `reciprocal` may therefore be interpreted as meaning: in those cases, if any, in which A interacts with B and B interacts with A, is the interaction strength guaranteed to be the same in both directions?

By default, the interaction strength is `1.0` for all interactions within `maxDistance`. Often it is desirable to change the interaction function using `setInteractionFunction()`; modifying interaction strengths can also be achieved with `interaction()` callbacks if necessary (see section 22.6). In any case, interactions beyond `maxDistance` always have a strength of `0.0`, and the interaction strength of an individual with itself is always `0.0`, regardless of the interaction function or callbacks.

The global symbol for the new interaction type is immediately available; the return value also provides the new object.

`(void)initializeMutationRate(numeric rates, [Ni ends = NULL], [string$ sex = "*"])`

Set the mutation rate per base position per generation along the chromosome. To be precise, this mutation rate is the expected mean number of mutations that will occur per base position per generation (per new offspring genome being generated); note that this is different from how the recombination rate is defined (see `initializeRecombinationRate()`). The number of mutations that actually occurs at a given base position when generating an offspring genome is, in effect, drawn from a Poisson distribution with that expected mean (but under the hood SLiM uses a mathematically equivalent but much more efficient strategy). It is possible for this Poisson draw to indicate that two or more new mutations have arisen at the same base position, particularly when the mutation rate is very high; in this case, the new mutations will be added to the site one at a time, and as always the mutation stacking policy (see section 1.5.3) will be followed.

There are two ways to call this function. If the optional `ends` parameter is `NULL` (the default), then `rates` must be a singleton value that specifies a single mutation rate to be used along the entire chromosome. If, on the other hand, `ends` is supplied, then `rates` and `ends` must be the same length, and the values in `ends` must be specified in ascending order. In that case, `rates` and `ends` taken together specify the mutation rates to be used along successive contiguous stretches of the chromosome, from beginning to end; the last position specified in `ends` should extend to the end of the chromosome (i.e. at least to the end of the last genomic element, if not further).

For example, if the following call is made:

```
initializeMutationRate(c(1e-7, 2.5e-8), c(5000, 9999));
```

then the result is that the mutation rate for bases `0`...`5000` (inclusive) will be `1e-7`, and the rate for bases `5001`...`9999` (inclusive) will be `2.5e-8`.

Note that mutations are generated by SLiM only within genomic elements, regardless of the mutation rate map. In effect, the mutation rate map given is intersected with the coverage area of the genomic elements defined; areas outside of any genomic element are given a mutation rate of zero. There is no harm in supplying a mutation rate map that specifies rates for areas outside of the genomic elements defined; that rate information is simply not used. The `overallMutationRate` family of properties on `Chromosome` provide the overall mutation rate after genomic element coverage has been taken into account, so it will reflect the rate at which new mutations will actually be generated in the simulation as configured.

If the optional sex parameter is "*" (the default), then the supplied mutation rate map will be used for both sexes (which is the only option for hermaphroditic simulations). In sexual simulations sex may be "M" or "F" instead, in which case the supplied mutation rate map is used only for that sex (i.e., when generating a gamete from a parent of that sex). In this case, two calls must be made to initializeMutationRate(), one for each sex, even if a rate of zero is desired for the other sex; no default mutation rate map is supplied.

```
(object<MutationType>$)initializeMutationType(is$ id, numeric$ dominanceCoeff,
    string$ distributionType, ...)
```

Add a mutation type at initialization time. The id must not already be used for any mutation type in the simulation. The id parameter may be either an integer giving the ID of the new mutation type, or a string giving the name of the new mutation type (such as "m5" to specify an ID of 5). The dominanceCoeff parameter supplies the dominance coefficient for the mutation type; 0.0 produces no dominance, 1.0 complete dominance, and values greater than 1.0, overdominance. The distributionType may be "f", in which case the ellipsis ... should supply a numeric$ fixed selection coefficient; "e", in which case the ellipsis should supply a numeric$ mean selection coefficient for an exponential distribution; "g", in which case the ellipsis should supply a numeric$ mean selection coefficient and a numeric$ alpha shape parameter for a gamma distribution; "n", in which case the ellipsis should supply a numeric$ mean selection coefficient and a numeric$ sigma (standard deviation) parameter for a normal distribution; "w", in which case the ellipsis should supply a numeric$ λ scale parameter and a numeric$ k shape parameter for a Weibull distribution; or "s", in which case the ellipsis should supply a string$ Eidos script parameter. See section 21.9 for discussion of the various DFEs and their uses. The global symbol for the new mutation type is immediately available; the return value also provides the new object.

Note that by default in WF models, all mutations of a given mutation type will be converted into Substitution objects when they reach fixation, for efficiency reasons. If you need to disable this conversion, to keep mutations of a given type active in the simulation even after they have fixed, you can do so by setting the convertToSubstitution property of MutationType to T.

In contrast, by default in nonWF models mutations will not be converted into Substitution objects when they reach fixation; convertToSubstitution is F by default in nonWF models. To enable conversion in nonWF models for neutral mutation types with no indirect fitness effects, you should therefore set convertToSubstitution to T.

See sections 18.3, 19.5, and 20.9.1 for further discussion regarding the convertToSubstitution property.

```
(void)initializeRecombinationRate(numeric rates, [Ni ends = NULL],
    [string$ sex = "*"])
```

Set the recombination rate per base position per generation along the chromosome. To be precise, this recombination rate is the probability that a breakpoint will occur between one base and the next base; note that this is different from how the mutation rate is defined (see initializeMutationRate()). All rates must be in the interval [0.0, 0.5]. A rate of 0.5 implies complete independence between the adjacent bases, which might be used to implement independent assortment of loci located on different chromosomes (see the example below). Whether a breakpoint occurs between two bases is then, in effect, determined by a binomial draw with a single trial and the given rate as probability (but under the hood SLiM uses a mathematically equivalent but much more efficient strategy). Unlike the mutational process in SLiM, then, which can generate more than one mutation at a given site (in one generation/genome), the recombinational process in SLiM will never generate more then one crossover between one base and the next (in one generation/genome), and a supplied rate of 0.5 will therefore result in an actual probability of 0.5 for a crossover at the relevant position. (Note that this was not true in SLiM 2.x and earlier, however; their implementation of recombination resulted in a crossover probability of about 39.3% for a rate of 0.5, due to the use of an inaccurate approximation method. Recombination rates lower than about 0.01 would have been essentially exact, since the approximation error became large only as the rate approached 0.5.)

There are two ways to call this function. If the optional `ends` parameter is `NULL` (the default), then `rates` must be a singleton value that specifies a single recombination rate to be used along the entire chromosome. If, on the other hand, `ends` is supplied, then `rates` and `ends` must be the same length, and the values in `ends` must be specified in ascending order. In that case, `rates` and `ends` taken together specify the recombination rates to be used along successive contiguous stretches of the chromosome, from beginning to end; the last position specified in `ends` should extend to the end of the chromosome (i.e. at least to the end of the last genomic element, if not further). Note that a recombination rate of 1 centimorgan/Mbp corresponds to a recombination rate of `1e-8` in the units used by SLiM.

For example, if the following call is made:

```
initializeRecombinationRate(c(0, 0.5, 0), c(5000, 5001, 9999));
```

then the result is that the recombination rates between bases `0` / `1`, `1` / `2`, ..., `4999` / `5000` will be `0`, the rate between bases `5000` / `5001` will be `0.5`, and the rate between bases `5001` / `5002` onward (up to `9998` / `9999`) will again be `0`. Setting the recombination rate between one specific pair of bases to `0.5` forces recombination to occur with a probability of `0.5` between those bases, which effectively breaks the simulated locus into separate chromosomes at that point; this example effectively has one simulated chromosome from base position `0` to `5000`, and another from `5001` to `9999`.

If the optional `sex` parameter is `"*"` (the default), then the supplied recombination rate map will be used for both sexes (which is the only option for hermaphroditic simulations). In sexual simulations `sex` may be `"M"` or `"F"` instead, in which case the supplied recombination map is used only for that sex. In this case, two calls must be made to `initializeRecombinationRate()`, one for each sex, even if a rate of zero is desired for the other sex; no default recombination map is supplied.

`(void)initializeSex(string$ chromosomeType, [numeric$ xDominanceCoeff = 1])`

Enable and configure sex in the simulation. The argument `chromosomeType` gives the type of chromosome to be simulated; this should be `"A"`, `"X"`, or `"Y"`. If the `chromosomeType` is `"X"`, the optional `xDominanceCoeff` parameter can supply the dominance coefficient used when a mutation is present in an XY male, and is thus "heterozygous" (but in a different sense than the heterozygosity of an XX female with one copy of the mutation). Calling this function has the side effect of enabling sex in the simulation; individuals will be male and female (rather than hermaphroditic) regardless of the `chromosomeType` chosen for simulation. There is no way to disable sex once it has been enabled; if you don't want to have sex, don't call this function.

`(void)initializeSLiMModelType(string$ modelType)`

Configure the type of SLiM model used for the simulation. At present, one of two model types may be selected. If `modelType` is `"WF"`, SLiM will use a Wright-Fisher (WF) model; this is the model type that has always been supported by SLiM, and is the model type used if `initializeSLiMModelType()` is not called. If `modelType` is `"nonWF"`, SLiM will use a non-Wright-Fisher (nonWF) model instead; this is a new model type supported by SLiM 3.0 and above (see section 1.6).

If `initializeSLiMModelType()` is called at all then it must be called before any other initialization function, so that SLiM knows from the outset which features are enabled and which are not.

```
(void)initializeSLiMOptions([logical$ keepPedigrees = F],
    [string$ dimensionality = ""], [string$ periodicity = ""],
    [integer$ mutationRuns = 0], [logical$ preventIncidentalSelfing = F])
```

Configure options for the simulation. If `initializeSLiMOptions()` is called at all then it must be called before any other initialization function (except `initializeSLiMModelType()`), so that SLiM knows from the outset which optional features are enabled and which are not.

If `keepPedigrees` is `T`, SLiM will keep pedigree information for every individual in the simulation, tracking the identity of its parents and grandparents. This allows individuals to assess their degree of pedigree-based relatedness to other individuals (see `Individual`'s `relatedness()` method, section 21.6.2), as well as allowing a model to find "trios" (two parents and an offspring they generated) using the pedigree properties of `Individual` (section 21.6.1). As a side effect of `keepPedigrees` being `T`, the `pedigreeID`, `pedigreeParentIDs`, and `pedigreeGrandparentIDs` properties of `Individual` will have defined values (see section 21.6.1), as will the `genomePedigreeID` property of `Genome` (see section 21.3.1). Note that pedigree-based relatedness doesn't necessarily correspond to genetic relatedness, due to effects such as assortment and recombination. For an overview of other ways of tracking genetic ancestry, including true local ancestry at each position on the chromosome, see section 13.9.

If `dimensionality` is not `""`, SLiM will enable its optional "continuous space" facility. Three values for `dimensionality` are presently supported: `"x"`, `"xy"`, and `"xyz"`, specifying that continuous space should be enabled for one, two, or three dimensions, respectively, using (*x*), (*x*, *y*), and (*x*, *y*, *z*) coordinates respectively. This has a number of side effects. First of all, it means that the specified properties of `Individual` (`x`, `y`, and/or `z`) will be interpreted by SLiM as spatial positions; in particular, SLiMgui will use those properties to display subpopulations spatially. Second, it allows spatial interactions to be defined, evaluated, and queried using `initializeInteractionType()` and `interaction()` callbacks. And third, it enables the use of any other properties and methods related to continuous space, such as setting the spatial boundaries of subpopulations, which would otherwise raise an error.

If `periodicity` is not `""`, SLiM will designate the specified spatial dimensions as being periodic – wrapping around at the edges of the spatial boundaries of that dimension. This option may only be used if the `dimensionality` parameter to `initializeSLiMOptions()` has been used to enable spatiality in the model, and only spatial dimensions that were specified in the dimensionality of the model may be declared to be periodic (but if desired, it is permissible to make just a subset of those dimensions periodic; it is not an all-or-none proposition). For example, if the specified dimensionality is `"xy"`, the model's periodicity may be `"x"`, `"y"`, or `"xy"` (or `""`, the default, to specify that there are no periodic dimensions). A one-dimensional periodic model would model a space like the perimeter of a circle. A two-dimensional model periodic in one of those dimensions would model a space like a cylinder without its end caps; if periodic in both dimensions, the modeled space is a torus. The shapes of three-dimensional periodic models are harder to visualize, but are essentially higher-dimensional analogues of these concepts. Periodic boundary conditions are commonly used to model spatial scenarios without "edge effects", since there are no edges in the periodic spatial dimensions. The `pointPeriodic()` method of `Subpopulation` is typically used in conjunction with this option, to actually implement the periodic boundary condition for the specified dimensions.

If `mutationRuns` is not `0`, SLiM will use the value given as the number of mutation runs inside `Genome` objects; if it is `0` (the default), SLiM will calculate a number of mutation runs that it estimates will work well. Internally, SLiM divides genomes into a sequence of consecutive mutation runs, allowing more efficient internal computations. The optimal mutation run length is short enough that each mutation run is relatively unlikely to be modified by mutation/recombination events when inherited, but long enough that each mutation run is likely to contain a relatively large number of mutations; these priorities are in tension, so an intermediate balance between them is generally desirable. The optimal number of mutation runs will depend upon the machine and even the compiler used to build SLiM, so SLiM's default value may not be optimal; for maximal performance it can thus be beneficial to experiment with different values and find the optimal value for the simulation – a process which SLiM can assist with (see section 18.4). Specifying the number of mutation runs is an advanced technique, but in certain cases it can improve performance significantly.

If `preventIncidentalSelfing` is `T`, incidental selfing in hermaphroditic models will be prevented by SLiM. By default (i.e., if `preventIncidentalSelfing` is `F`), SLiM chooses the first and second parents in a biparental mating event independently. It is therefore possible for the same individual to be chosen as both the first and second parent, resulting in selfing events even when the selfing rate is zero. In many models this is unimportant, since it happens fairly infrequently and does not have large consequences. This behavior is SLiM's default because it is the simplest option, and produces results that most closely align with simple analytical population genetics models. However, in some models this selfing can be undesirable and problematic. In particular, models that involve very high variance in fitness or very small effective population sizes may see elevated rates of selfing that substantially influence model results. If `preventIncidentalSelfing` is set to `T`, all such incidental selfing will be prevented (by choosing a new second parent if the first parent was chosen again). Non-incidental selfing, as requested by the selfing rate, will still be permitted. Note that if incidental selfing is prevented, SLiM will hang if it is unable to find a different second parent; there must always be at least two individuals in the population with non-zero fitness, and `mateChoice()` and `modifyChild()` callbacks must not absolutely prevent those two individuals from producing viable offspring. Enforcement of the prohibition on incidental selfing will occur after `mateChoice()` callbacks have been called (and thus the default mating weights provided to `mateChoice()` callbacks will *not* exclude the first parent!), but will occur before `modifyChild()` callbacks are called (so those callbacks may assume that the first and second parents are distinct).

This function will likely be extended with further options in the future, added on to the end of the argument list. Using named arguments with this call is recommended for readability. Note that turning on optional features may increase the runtime and memory footprint of SLiM.

```
(void)initializeTreeSeq([logical$ recordMutations = T],
    [float$ simplificationRatio = 10], [logical$ checkCoalescence = F],
    [logical$ runCrosschecks = F])
```

Configure options for tree sequence recording. Calling this function turns on tree sequence recording, as a side effect, for later reconstruction of the simulation's evolutionary dynamics; if you do not want tree sequence recording to be enabled, do not call this function.

The `recordMutations` flag controls whether information about individual mutations is recorded or not. Such recording takes time and memory, and so can be turned off if only the tree sequence itself is needed, but it is turned on by default since mutation recording is generally useful.

The `simplificationRatio` parameter controls how often automatic simplification of the recorded tree sequence occurs. This is a speed–memory tradeoff: more frequent simplification (lower `simplificationRatio`) means the stored tree sequences will use less memory, but at a cost of somewhat longer run times. Conversely, a larger `simplificationRatio` means that SLiM will wait longer between simplifications. SLiM will try to find an optimal generation interval for simplification such that the ratio of the memory used by the tree sequence tables, (before:after) simplification, is close to the requested ratio. The default of `10` thus requests that SLiM try to find a generation interval such that the maximum size of the stored tree sequences is ten times the size after simplification. `INF` may be supplied as a special value indicating that automatic simplification should never occur; `0` may be supplied to indicate that automatic simplification should be performed at the end of every generation.

The `checkCoalescence` parameter controls whether a check for full coalescence is conducted after each simplification. If a model will call `treeSeqCoalesced()` to check for coalescence during its execution, `checkCoalescence` should be set to `T`. Since the coalescence checks entail a performance penalty, the default of `F` is preferable otherwise. See the documentation for `treeSeqCoalesced()` for further discussion.

The `runCrosschecks` parameter controls whether cross-checks between SLiM's internal data structures and the tree-sequence recording data structures will be conducted. These two sets of data structures record much the same thing (mutations in genomes), but using completely different representations, so such cross-checks can be useful to confirm that the two data structures do indeed represent the same conceptual state. This slows down the model considerably, however, and would normally be turned on only for debugging purposes, so it is turned off by default.

Once all `initialize()` callbacks have executed, in the order in which they are specified in the SLiM input file, the simulation will begin. The generation number at which it starts is determined by the Eidos events you have defined (see section 22.1); the first generation in which an Eidos event is scheduled to execute is the generation at which the simulation starts. Similarly, the simulation will terminate after the last generation for which a script block (either an event or a callback) is registered to execute, unless the `stop()` function is called to end the simulation earlier.

21.2 Class Chromosome

This class represents the layout and properties of the chromosome being simulated. The chromosome currently being simulated is available through the `sim.chromosome` global. Section 1.5.4 presents an overview of the conceptual role of this class.

21.2.1 `Chromosome` properties

`colorSubstitution <–> (string$)`

The color used to display substitutions in SLiMgui when both mutations and substitutions are being displayed in the chromosome view. Outside of SLiMgui, this property still exists, but is not used by SLiM. Colors may be specified by name, or with hexadecimal RGB values of the form `"#RRGGBB"` (see the Eidos manual). If `colorSubstitution` is the empty string, `""`, SLiMgui will defer to the color scheme of each `MutationType`, just as it does when only substitutions are being displayed. The default, `"3333FF"`, causes all substitutions to be shown as dark blue when displayed in conjunction with mutations, to prevent the view from becoming too noisy. Note that when substitutions are displayed without mutations also being displayed, this value is ignored by SLiMgui and the substitutions use the color scheme of each `MutationType`.

`geneConversionFraction <–> (float$)`

The fraction of crossover events that result in gene conversion; see SLiM's manual for details.

`geneConversionMeanLength <–> (float$)`

The mean length of a gene conversion event (in base positions).

`genomicElements => (object<GenomicElement>)`

All of the `GenomicElement` objects that comprise the chromosome.

`lastPosition => (integer$)`

The last valid position in the chromosome; its length, essentially.

`mutationEndPositions => (integer)`

The end positions for mutation rate regions along the chromosome. Each mutation rate region is assumed to start at the position following the end of the previous mutation rate region; in other words, the regions are assumed to be contiguous. When using sex-specific mutation rate maps, this property will unavailable; see `mutationEndPositionsF` and `mutationEndPositionsM`.

`mutationEndPositionsF => (integer)`

The end positions for mutation rate regions for females, when using sex-specific mutation rate maps; unavailable otherwise. See `mutationEndPositions` for further explanation.

`mutationEndPositionsM => (integer)`

The end positions for mutation rate regions for males, when using sex-specific mutation rate maps; unavailable otherwise. See `mutationEndPositions` for further explanation.

`mutationRates => (float)`

The mutation rate for each of the mutation rate regions specified by `mutationEndPositions`. When using sex-specific mutation rate maps, this property will be unavailable; see `mutationRatesF` and `mutationRatesM`.

`mutationRatesF => (float)`

The mutation rate for each of the mutation rate regions specified by `mutationEndPositionsF`, when using sex-specific mutation rate maps; unavailable otherwise.

`mutationRatesM => (float)`

The mutation rate for each of the mutation rate regions specified by `mutationEndPositionsM`, when using sex-specific mutation rate maps; unavailable otherwise.

`overallMutationRate => (float$)`

The overall mutation rate across the whole chromosome determining the overall number of mutation events that will occur anywhere in the chromosome, as calculated from the individual mutation ranges and rates as well as the coverage of the chromosome by genomic elements (since mutations are only generated within genomic elements, regardless of the mutation rate map). When using sex-specific mutation rate maps, this property will unavailable; see `overallMutationRateF` and `overallMutationRateM`.

`overallMutationRateF => (float$)`

The overall mutation rate for females, when using sex-specific mutation rate maps; unavailable otherwise. See `overallMutationRate` for further explanation.

`overallMutationRateM => (float$)`

The overall mutation rate for males, when using sex-specific mutation rate maps; unavailable otherwise. See `overallMutationRate` for further explanation.

`overallRecombinationRate => (float$)`

The overall recombination rate across the whole chromosome determining the overall number of recombination events that will occur anywhere in the chromosome, as calculated from the individual recombination ranges and rates. When using sex-specific recombination maps, this property will unavailable; see `overallRecombinationRateF` and `overallRecombinationRateM`.

`overallRecombinationRateF => (float$)`

The overall recombination rate for females, when using sex-specific recombination maps; unavailable otherwise. See `overallRecombinationRate` for further explanation.

`overallRecombinationRateM => (float$)`

The overall recombination rate for males, when using sex-specific recombination maps; unavailable otherwise. See `overallRecombinationRate` for further explanation.

`recombinationEndPositions => (integer)`

The end positions for recombination regions along the chromosome. Each recombination region is assumed to start at the position following the end of the previous recombination region; in other words, the regions are assumed to be contiguous. When using sex-specific recombination maps, this property will unavailable; see `recombinationEndPositionsF` and `recombinationEndPositionsM`.

`recombinationEndPositionsF => (integer)`

The end positions for recombination regions for females, when using sex-specific recombination maps; unavailable otherwise. See `recombinationEndPositions` for further explanation.

`recombinationEndPositionsM => (integer)`

The end positions for recombination regions for males, when using sex-specific recombination maps; unavailable otherwise. See `recombinationEndPositions` for further explanation.

`recombinationRates => (float)`

The recombination rate for each of the recombination regions specified by `recombinationEndPositions`. When using sex-specific recombination maps, this property will unavailable; see `recombinationRatesF` and `recombinationRatesM`.

`recombinationRatesF => (float)`

The recombination rate for each of the recombination regions specified by `recombinationEndPositionsF`, when using sex-specific recombination maps; unavailable otherwise.

`recombinationRatesM => (float)`

The recombination rate for each of the recombination regions specified by `recombinationEndPositionsM`, when using sex-specific recombination maps; unavailable otherwise.

`tag <–> (integer$)`

A user-defined `integer` value. The value of `tag` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code. The value of `tag` is not used by SLiM; it is free for you to use.

21.2.2 `Chromosome` methods

`– (integer)drawBreakpoints([No<Individual>$ parent = NULL], [Ni$ n = NULL])`

Draw recombination breakpoints, using the chromosome's recombination rate map, the current gene conversion parameters, and (in some cases – see below) any active and applicable `recombination()` callbacks. The number of breakpoints to generate, `n`, may be supplied; if it is `NULL` (the default), the number of breakpoints will be drawn based upon the overall recombination rate and the chromosome length (following the standard procedure in SLiM). Note that if gene conversion is enabled, the number of breakpoints generated may not be equal to the number requested, because any given breakpoint might become a gene conversion event, which entails an additional breakpoint (to terminate the gene conversion tract).

It is generally recommended that the parent individual be supplied to this method, but `parent` is `NULL` by default. The individual supplied in `parent` is used for two purposes. First, in sexual models that define separate recombination rate maps for males versus females, the sex of `parent` will be used to determine which map is used; in this case, a non-`NULL` value *must* be supplied for `parent`, since the choice of recombination rate map must be determined. Second, in models that define `recombination()` callbacks, `parent` is used to determine the various pseudo-parameters that are passed to `recombination()` callbacks (`individual`, `genome1`, `genome2`, `subpop`), and the subpopulation to which `parent` belongs is used to select which `recombination()` callbacks are applicable; given the necessity of this information, `recombination()` callbacks will not be called as a side effect of this method if `parent` is `NULL`. Apart from these two uses, `parent` is not used, and the caller does not guarantee that the generated breakpoints will actually be used to recombine the genomes of `parent` in particular.

`– (void)setMutationRate(numeric rates, [Ni ends = NULL], [string$ sex = "*"])`

Set the mutation rate per base position per generation along the chromosome. There are two ways to call this method. If the optional `ends` parameter is `NULL` (the default), then `rates` must be a singleton value that specifies a single mutation rate to be used along the entire chromosome. If, on the other hand, `ends` is supplied, then `rates` and `ends` must be the same length, and the values in `ends` must be specified in ascending order. In that case, `rates` and `ends` taken together specify the mutation rates to be used along successive contiguous stretches of the chromosome, from beginning to end; the last position specified in `ends` should extend to the end of the chromosome (as previously determined, during simulation initialization). See the `initializeMutationRate()` function for further discussion of precisely how these rates and positions are interpreted.

If the optional `sex` parameter is `"*"` (the default), then the supplied mutation rate map will be used for both sexes (which is the only option for hermaphroditic simulations). In sexual simulations `sex` may be `"M"` or `"F"` instead, in which case the supplied mutation rate map is used only for that sex. Note that whether sex-specific mutation rate maps will be used is set by the way that the simulation is initially configured with `initializeMutationRate()`, and cannot be changed with this method; so if the simulation was set up to use sex-specific mutation rate maps then sex must be `"M"` or `"F"` here, whereas if it was set up not to, then sex must be `"*"` or unsupplied here. If a simulation needs sex-specific mutation rate maps only some of the time, the male and female maps can simply be set to be identical the rest of the time.

The mutation rate intervals are normally a constant in simulations, so be sure you know what you are doing.

– `(void)setRecombinationRate(numeric rates, [Ni ends = NULL], [string$ sex = "*"])`

Set the recombination rate per base position per generation along the chromosome. All rates must be in the interval [`0.0`, `0.5`]. There are two ways to call this method. If the optional `ends` parameter is `NULL` (the default), then `rates` must be a singleton value that specifies a single recombination rate to be used along the entire chromosome. If, on the other hand, `ends` is supplied, then `rates` and `ends` must be the same length, and the values in `ends` must be specified in ascending order. In that case, `rates` and `ends` taken together specify the recombination rates to be used along successive contiguous stretches of the chromosome, from beginning to end; the last position specified in `ends` should extend to the end of the chromosome (as previously determined, during simulation initialization). See the `initializeRecombinationRate()` function for further discussion of precisely how these rates and positions are interpreted.

If the optional `sex` parameter is `"*"` (the default), then the supplied recombination rate map will be used for both sexes (which is the only option for hermaphroditic simulations). In sexual simulations `sex` may be `"M"` or `"F"` instead, in which case the supplied recombination map is used only for that sex. Note that whether sex-specific recombination maps will be used is set by the way that the simulation is initially configured with `initializeRecombinationRate()`, and cannot be changed with this method; so if the simulation was set up to use sex-specific recombination maps then sex must be `"M"` or `"F"` here, whereas if it was set up not to, then sex must be `"*"` or unsupplied here. If a simulation needs sex-specific recombination maps only some of the time, the male and female maps can simply be set to be identical the rest of the time.

The recombination intervals are normally a constant in simulations, so be sure you know what you are doing.

21.3 Class Genome

This class represents one full genome of an individual (one of the two genomes contained by a diploid individual, that is, in the way that SLiM uses the term), composed of the mutations carried by that individual. Section 1.5.1 presents an overview of the conceptual role of this class.

21.3.1 `Genome` properties

`genomePedigreeID => (integer$)`

If pedigree tracking is turned on with `initializeSLiMOptions(keepPedigrees=T)`, `genomePedigreeID` is a unique non-negative identifier for each genome in a simulation, never re-used throughout the duration of the simulation run. Furthermore, the `genomePedigreeID` of a given genome will be equal to either `(2*pedigreeID)` or `(2*pedigreeID + 1)` of the individual that the genome belongs to (the former for the first genome of the individual, the latter for the second genome of the individual); this invariant relationship is guaranteed. If pedigree tracking is not on, the value of `genomePedigreeID` will be a singleton `-1`.

`genomeType => (string$)`

The type of chromosome represented by this genome; one of `"A"`, `"X"`, or `"Y"`.

`isNullGenome => (logical$)`

`T` if the genome is a "null" genome, `F` if it is an ordinary genome object. When a sex chromosome (X or Y) is simulated, the other sex chromosome also exists in the simulation, but it is a "null" genome that does not carry any mutations. Instead, it is a placeholder, present to allow SLiM's code to operate in much the same way as it does when an autosome is simulated. Null genomes should not be accessed or manipulated.

`mutations => (object<Mutation>)`

All of the `Mutation` objects present in this genome.

`tag <–> (integer$)`

A user-defined `integer` value. The value of `tag` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code. The value of `tag` is not used by SLiM; it is free for you to use.

Note that the `Genome` objects used by SLiM are new with every generation, so the `tag` value of each new offspring generated in each generation will be initially undefined. If you set a `tag` value for an offspring genome inside a `modifyChild()` callback, that `tag` value will be preserved as the offspring individual becomes a parent (across the generation boundary, in other words). If you take advantage of this, however, you should be careful to set up initial values for the tag values of *all* offspring, otherwise undefined initial values might happen to match the values that you are trying to use to tag particular individuals. A rule of thumb in programming: undefined values should always be assumed to take on the most inconvenient value possible.

21.3.2 `Genome` methods

`+ (void)addMutations(object<Mutation> mutations)`

Add the existing mutations in `mutations` to the genome, if they are not already present (if they are already present, they will be ignored), and if the addition is not prevented by the mutation stacking policy (see the `mutationStackPolicy` property of `MutationType`, section 21.9.1).

Calling this will normally affect the fitness values calculated at the end of the current generation; if you want current fitness values to be affected, you can call `SLiMSim`'s method `recalculateFitness()` – but see the documentation of that method for caveats.

```
+ (object<Mutation>)addNewDrawnMutation(io<MutationType> mutationType,
    integer position, [Ni originGeneration = NULL],
    [Nio<Subpopulation> originSubpop = NULL])
```

Add new mutations to the target genome(s) with the specified `mutationType` (specified by the `MutationType` object or by `integer` identifier), `position`, `originGeneration` (which may be `NULL`, the default, to specify the current generation), and `originSubpop` (specified by the `Subpopulation` object or by `integer` identifier, or by `NULL`, the default, to specify the subpopulation to which the first target genome belongs). If `originSubpop` is supplied as an `integer`, it is intentionally not checked for validity; you may use arbitrary values of `originSubpop` to "tag" the mutations that you create (see section 21.8.1). The selection coefficients of the mutations are drawn from their mutation types; `addNewMutation()` may be used instead if you wish to specify selection coefficients.

Beginning in SLiM 2.5 this method is vectorized, so all of these parameters may be singletons (in which case that single value is used for all mutations created by the call) or non-singleton vectors (in which case one element is used for each corresponding mutation created). Non-singleton parameters must match in length, since their elements need to be matched up one-to-one.

The new mutations created by this method are returned, even if their actual addition is prevented by the mutation stacking policy (see the `mutationStackPolicy` property of `MutationType`, section 21.9.1). However, the order of the mutations in the returned vector is not guaranteed to be the same as the order in which the values are specified in parameter vectors, unless the `position` parameter is specified in ascending order. In other words, pre-sorting the parameters to this method into ascending order by position, using `order()` and subsetting, will guarantee that the order of the returned vector of mutations corresponds to the order of elements in the parameters to this method; otherwise, no such guarantee exists.

Beginning in SLiM 2.1, this is a class method, not an instance method. This means that it does not get multiplexed out to all of the elements of the receiver (which would add a different new mutation to each element); instead, it is performed as a single operation, adding the same new mutation objects to all of the elements of the receiver. Before SLiM 2.1, to add the same mutations to multiple genomes, it was necessary to call `addNewDrawnMutation()` on one of the genomes, and then add the returned `Mutation` object to all of the other genomes using `addMutations()`. That is not necessary in SLiM 2.1 and later, because of this change (although doing it the old way does no harm and produces identical behavior). Pre-2.1 code that actually relied upon the old multiplexing behavior will no longer work correctly (but this is expected to be an extremely rare pattern of usage).

Calling this will normally affect the fitness values calculated at the end of the current generation (but not sooner); if you want current fitness values to be affected, you can call `SLiMSim`'s method `recalculateFitness()` – but see the documentation of that method for caveats.

```
+ (object<Mutation>)addNewMutation(io<MutationType> mutationType,
    numeric selectionCoeff, integer position, [Ni originGeneration = NULL],
    [Nio<Subpopulation> originSubpop = NULL])
```

Add new mutations to the target genome(s) with the specified `mutationType` (specified by the `MutationType` object or by `integer` identifier), `selectionCoeff`, `position`, `originGeneration` (which may be `NULL`, the default, to specify the current generation), and `originSubpop` (specified by the `Subpopulation` object or by `integer` identifier, or by `NULL`, the default, to specify the subpopulation to which the first target genome belongs). If `originSubpop` is supplied as an `integer`, it is intentionally not checked for validity; you may use arbitrary values of `originSubpop` to "tag" the mutations that you create (see section 21.8.1). The `addNewDrawnMutation()` method may be used instead if you wish selection coefficients to be drawn from the mutation types of the mutations.

The new mutations created by this method are returned, even if their actual addition is prevented by the mutation stacking policy (see the `mutationStackPolicy` property of `MutationType`, section 21.9.1). However, the order of the mutations in the returned vector is not guaranteed to be the same as the order in which the values are specified in parameter vectors, unless the `position` parameter is specified in ascending order. In other words, pre-sorting the parameters to this method into ascending order by position, using `order()` and subsetting, will guarantee that the order of the returned vector of mutations corresponds to the order of elements in the parameters to this method; otherwise, no such guarantee exists.

Beginning in SLiM 2.1, this is a class method, not an instance method. This means that it does not get multiplexed out to all of the elements of the receiver (which would add a different new mutation to each element); instead, it is performed as a single operation, adding the same new mutation object to all of the elements of the receiver. Before SLiM 2.1, to add the same mutation to multiple genomes, it was necessary to call `addNewMutation()` on one of the genomes, and then add the returned `Mutation` object to all of the other genomes using `addMutations()`. That is not necessary in SLiM 2.1 and later, because of this change (although doing it the old way does no harm and produces identical behavior). Pre-2.1 code that actually relied upon the old multiplexing behavior will no longer work correctly (but this is expected to be an extremely rare pattern of usage).

Calling this will normally affect the fitness values calculated at the end of the current generation (but not sooner); if you want current fitness values to be affected, you can call `SLiMSim`'s method `recalculateFitness()` – but see the documentation of that method for caveats.

– `(Nlo<Mutation>$)containsMarkerMutation(io<MutationType>$ mutType, integer$ position, [logical$ returnMutation = F])`

Returns `T` if the genome contains a mutation of type `mutType` at `position`, `F` otherwise (if `returnMutation` has its default value of `F`; see below). This method is, as its name suggests, intended for checking for "marker mutations": mutations of a special mutation type that are not literally mutations in the usual sense, but instead are added in to particular genomes to mark them as possessing some property. Marker mutations are not typically added by SLiM's mutation-generating machinery; instead they are added explicitly with `addNewMutation()` or `addNewDrawnMutation()` at a known, constant position in the genome. This method provides a check for whether a marker mutation of a given type exists in a particular genome; because the position to check is known in advance, that check can be done much faster than the equivalent check with `containsMutations()` or `countOfMutationsOfType()`, using a binary search of the genome. See section 13.5 for one example of a model that uses marker mutations – in that case, to mark chromosomes that possess an inversion.

If `returnMutation` is `T` (an option added in SLiM 3), this method returns the actual mutation found, rather than just `T` or `F`. More specifically, the *first* mutation found of `mutType` at `position` will be returned; if more than one such mutation exists in the target genome, which one is returned is not defined. If `returnMutation` is T and no mutation of `mutType` is found at `position`, `NULL` will be returned.

– `(logical)containsMutations(object<Mutation> mutations)`

Returns a `logical` vector indicating whether each of the mutations in `mutations` is present in the genome; each element in the returned vector indicates whether the corresponding mutation is present (`T`) or absent (`F`). This method is provided for speed; it is much faster than the corresponding Eidos code.

– `(integer$)countOfMutationsOfType(io<MutationType>$ mutType)`

Returns the number of mutations that are of the type specified by `mutType`, out of all of the mutations in the genome. If you need a vector of the matching `Mutation` objects, rather than just a count, use `–mutationsOfType()`. This method is provided for speed; it is much faster than the corresponding Eidos code.

– `(object<Mutation>)mutationsOfType(io<MutationType>$ mutType)`

Returns an `object` vector of all the mutations that are of the type specified by `mutType`, out of all of the mutations in the genome. If you just need a count of the matching `Mutation` objects, rather than a vector of the matches, use `–countOfMutationsOfType()`; if you need just the positions of matching `Mutation` objects, use `–positionsOfMutationsOfType()`; and if you are aiming for a sum of the selection coefficients of matching `Mutation` objects, use `–sumOfMutationsOfType()`. This method is provided for speed; it is much faster than the corresponding Eidos code.

+ `(void)output([Ns$ filePath = NULL], [logical$ append = F])`

Output the target genomes in SLiM's native format (see section 23.3.1 for output format details). This low-level output method may be used to output any sample of `Genome` objects (the Eidos function `sample()` may be useful for constructing custom samples, as may the SLiM class `Individual`). For output of a sample from a single `Subpopulation`, the `outputSample()` of `Subpopulation` may be more straightforward to use. If the optional parameter `filePath` is `NULL` (the default), output is directed to SLiM's standard output. Otherwise, the output is sent to the file specified by `filePath`, overwriting that file if `append` if `F`, or appending to the end of it if `append` is `T`.

See `outputMS()` and `outputVCF()` for other output formats. Output is generally done in a `late()` event, so that the output reflects the state of the simulation at the end of a generation.

```
+ (void)outputMS([Ns$ filePath = NULL], [logical$ append = F],
    [logical$ filterMonomorphic = F])
```

Output the target genomes in MS format (see section 23.3.2 for output format details). This low-level output method may be used to output any sample of `Genome` objects (the Eidos function `sample()` may be useful for constructing custom samples, as may the SLiM class `Individual`). For output of a sample from a single `Subpopulation`, the `outputMSSample()` of `Subpopulation` may be more straightforward to use. If the optional parameter `filePath` is `NULL` (the default), output is directed to SLiM's standard output. Otherwise, the output is sent to the file specified by `filePath`, overwriting that file if `append` if `F`, or appending to the end of it if `append` is `T`. Positions in the output will span the interval [0,1].

If `filterMonomorphic` is `F` (the default), all mutations that are present in the sample will be included in the output. This means that some mutations may be included that are actually monomorphic within the sample (i.e., that exist in *every* sampled genome, and are thus apparently fixed). These may be filtered out with `filterMonomorphic = T` if desired; note that this option means that some mutations that do exist in the sampled genomes might not be included in the output, simply because they exist in every sampled genome.

See `output()` and `outputVCF()` for other output formats. Output is generally done in a `late()` event, so that the output reflects the state of the simulation at the end of a generation.

```
+ (void)outputVCF([Ns$ filePath = NULL], [logical$ outputMultiallelics = T],
    [logical$ append = F])
```

Output the target genomes in VCF format (see section 23.3.3 for output format details). The target genomes are treated as pairs comprising individuals for purposes of structuring the VCF output, so an even number of genomes is required. This low-level output method may be used to output any sample of `Genome` objects (the Eidos function `sample()` may be useful for constructing custom samples, as may the SLiM class `Individual`). For output of a sample from a single `Subpopulation`, the `outputVCFSample()` of `Subpopulation` may be more straightforward to use. If the optional parameter `filePath` is `NULL` (the default), output is directed to SLiM's standard output. Otherwise, the output is sent to the file specified by `filePath`, overwriting that file if `append` if `F`, or appending to the end of it if `append` is `T`.

In SLiM, it is often possible for a single individual to have multiple mutations at a given base position. Because the VCF format is an explicit-nucleotide format, this property of SLiM does not fit well into VCF. Since there are only four possible nucleotides at a given base position in VCF, at most one "reference" state and three "alternate" states could be represented at that base position. SLiM, on the other hand, can represent any number of alternative possibilities at a given base; in general, if N different mutations are segregating at a given position, there are 2^N different allelic states at that position in SLiM. For this reason, SLiM does not attempt to represent multiple mutations at a single site as being alternative alleles in a single output line, as is typical in VCF format. Instead, SLiM produces a separate line of VCF output for each segregating mutation at a given position. SLiM always declares base positions as having a "reference base" of `A` (representing the state in individuals that do not carry a given mutation) and an "alternate base" of `T` (representing the state in individuals that do carry the given mutation). Multiallelic positions will thus produce VCF output showing multiple `A`-to-`T` changes at the same position, possessed by different but possibly overlapping sets of individuals. Many programs that process VCF output may not behave correctly with this style of output. SLiM therefore provides a choice, using the `outputMultiallelics` flag; if that flag is `T` (the default), SLiM will produce multiple lines of output for multiallelic base positions, but will mark those lines with a `MULTIALLELIC` flag in the `INFO` field of the VCF output so that those lines can be filtered or processed in a special manner. If `outputMultiallelics` is `F`, on the other hand, SLiM will completely suppress output of all mutations at multiallelic sites – often the simplest option, if doing so does not lead to bias in the subsequent analysis. This flag has no effect upon the output of sites with only a single mutation present. Assessment of whether a site is multiallelic is done only within the sample; segregating mutations that are not part of the sample are ignored.

See `outputMS()` and `output()` for other output formats. Output is generally done in a `late()` event, so that the output reflects the state of the simulation at the end of a generation.

`– (integer)positionsOfMutationsOfType(io<MutationType>$ mutType)`

Returns the positions of mutations that are of the type specified by `mutType`, out of all of the mutations in the genome. If you need a vector of the matching `Mutation` objects, rather than just positions, use `-mutationsOfType()`. This method is provided for speed; it is much faster than the corresponding Eidos code.

`+ (void)removeMutations([No<Mutation> mutations = NULL], [logical$ substitute = F])`

Remove the mutations in `mutations` from the target genome(s), if they are present (if they are not present, they will be ignored). If `NULL` is passed for `mutations` (which is the default), then all mutations will be removed from the target genomes; in this case, `substitute` must be `F` (a specific vector of mutations to be substituted is required). Note that the `Mutation` objects removed remain valid, and will still be in the simulation's mutation registry (i.e. will be returned by `SLiMSim`'s `mutations` property), until the next generation.

Changing this will normally affect the fitness values calculated at the end of the current generation; if you want current fitness values to be affected, you can call `SLiMSim`'s method `recalculateFitness()` – but see the documentation of that method for caveats.

The optional parameter `substitute` was added in SLiM 2.2, with a default of `F` for backward compatibility. If `substitute` is `T`, `Substitution` objects will be created for all of the removed mutations so that they are recorded in the simulation as having fixed, just as if they had reached fixation and been removed by SLiM's own internal machinery. This will occur regardless of whether the mutations have in fact fixed, regardless of the `convertToSubstitution` property of the relevant mutation types, and regardless of whether all copies of the mutations have even been removed from the simulation (making it possible to create `Substitution` objects for mutations that are still segregating). It is up to the caller to perform whatever checks are necessary to preserve the integrity of the simulation's records. Typically `substitute` will only be set to `T` in the context of calls like `sim.subpopulations.genomes.removeMutations(muts, T)`, such that the substituted mutations are guaranteed to be entirely removed from circulation. As mentioned above, `substitute` may not be `T` if `mutations` is `NULL`.

`– (float$)sumOfMutationsOfType(io<MutationType>$ mutType)`

Returns the sum of the selection coefficients of all mutations that are of the type specified by `mutType`, out of all of the mutations in the genome. This is often useful in models that use a particular mutation type to represent QTLs with additive effects; in that context, `sumOfMutationsOfType()` will provide the sum of the additive effects of the QTLs for the given mutation type. This method is provided for speed; it is much faster than the corresponding Eidos code. Note that this method also exists on `Individual`, for cases in which the sum across both genomes of an individual is desired.

21.4 Class GenomicElement

This class represents a genomic element of a particular genomic element type, with a start and end; the chromosome is composed of a series of such genomic elements. Section 1.5.4 presents an overview of the conceptual role of this class.

21.4.1 `GenomicElement` properties

`endPosition => (integer$)`

The last position in the chromosome contained by this genomic element.

`genomicElementType => (object<GenomicElementType>$)`

The `GenomicElementType` object that defines the behavior of this genomic element.

`startPosition => (integer$)`

The first position in the chromosome contained by this genomic element.

`tag <–> (integer$)`

A user-defined `integer` value. The value of `tag` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code. The value of `tag` is not used by SLiM; it is free for you to use.

21.4.2 `GenomicElement` methods

`– (void)setGenomicElementType(io<GenomicElementType>$ genomicElementType)`

Set the genomic element type used for a genomic element (see sections 1.3 and 4.1.5). The genomicElementType parameter should supply the new genomic element type for the element, either as a `GenomicElementType` object or as an `integer` identifier. The genomic element type for a genomic element is normally a constant in simulations, so be sure you know what you are doing.

21.5 Class GenomicElementType

This class represents a type of genomic element, with particular mutation types. The genomic element types currently defined in the simulation are defined as global constants with the same names used in the SLiM input file – `g1`, `g2`, and so forth. Section 1.5.4 presents an overview of the conceptual role of this class.

21.5.1 `GenomicElementType` properties

`color <–> (string$)`

The color used to display genomic elements of this type in SLiMgui. Outside of SLiMgui, this property still exists, but is not used by SLiM. Colors may be specified by name, or with hexadecimal RGB values of the form `"#RRGGBB"` (see the Eidos manual). If `color` is the empty string, `""`, SLiMgui's default color scheme is used; this is the default for new `GenomicElementType` objects.

`id => (integer$)`

The identifier for this genomic element type; for genomic element type `g3`, for example, this is `3`.

`mutationFractions => (float)`

For each `MutationType` represented in this genomic element type, this property has the corresponding fraction of all mutations that will be drawn from that `MutationType`.

`mutationTypes => (object<MutationType>)`

The `MutationType` instances used by this genomic element type.

`tag <–> (integer$)`

A user-defined `integer` value. The value of `tag` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code. The value of `tag` is not used by SLiM; it is free for you to use. See also the `getValue()` and `setValue()` methods, for another way of attaching state to genomic element types.

21.5.2 `GenomicElementType` methods

`– (+)getValue(string$ key)`

Returns the value previously set for the dictionary entry identifier `key` using `setValue()`, or `NULL` if no value has been set. This dictionary-style functionality is actually provided by the superclass of `GenomicElementType`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

– `(void)setMutationFractions(io<MutationType> mutationTypes, numeric proportions)`

Set the mutation type fractions contributing to a genomic element type. The `mutationTypes` vector should supply the mutation types used by the genomic element (either as `MutationType` objects or as `integer` identifiers), and the `proportions` vector should be of equal length, specifying the relative proportion of mutations that will be draw from each corresponding type (see sections 1.3 and 4.1.3). This is normally a constant in simulations, so be sure you know what you are doing.

– `(void)setValue(string$ key, + value)`

Sets a value for the dictionary entry identifier `key`. The value, which may be of any type other than `object`, can be fetched later using `getValue()`. This dictionary-style functionality is actually provided by the superclass of `GenomicElementType`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

21.6 Class Individual

This class represents a single simulated individual. Individuals in SLiM are diploid, and thus contain two `Genome` objects. Most functionality in SLiM is contained in the `Genome` class; the `Individual` class is mostly a convenient way to treat the pairs of genomes associated with an individual as a single object, and to associate a `tag` value with individuals. Section 1.5.1 presents an overview of the conceptual role of this class.

21.6.1 `Individual` properties

`age <–> (integer$)`

The age of the individual, measured in generation "ticks". A newly generated offspring individual will have an age of `0` in the same generation in which is was created. The age of every individual is incremented by one at the same point that the generation counter is incremented. The age of individuals may be changed; usually this only makes sense when setting up the initial state of a model, however.

`color <–> (string$)`

The color used to display the individual in SLiMgui. Outside of SLiMgui, this property still exists, but is not used by SLiM. Colors may be specified by name, or with hexadecimal RGB values of the form `"#RRGGBB"` (see the Eidos manual). If `color` is the empty string, `""`, SLiMgui's default (fitness-based) color scheme is used; this is the default for new `Individual` objects.

`fitnessScaling <–> (float$)`

A `float` scaling factor applied to the individual's fitness (i.e., the fitness value computed for the individual will be multiplied by this value). This provides a simple, fast way to modify the fitness of an individual; conceptually it is similar to returning a fitness effect for the individual from a `fitness(NULL)` callback, but without the complexity and performance overhead of implementing such a callback. To scale the fitness of all individuals in a subpopulation by the same factor, see the `fitnessScaling` property of `Subpopulation`.

The value of `fitnessScaling` is reset to `1.0` every generation, so that any scaling factor set lasts for only a single generation. This reset occurs immediately after fitness values are calculated, in both WF and nonWF models.

`genomes => (object<Genome>)`

The pair of `Genome` objects associated with this individual. If only one of the two genomes is desired, the `genome1` or `genome2` property may be used.

`genome1 => (object<Genome>$)`

The first `Genome` object associated with this individual. This property is particularly useful when you want the first genome from each of a vector of individuals, as often arises in haploid models.

`genome2 => (object<Genome>$)`

The second `Genome` object associated with this individual. This property is particularly useful when you want the second genome from each of a vector of individuals, as often arises in haploid models.

`index => (integer$)`

The index of the individual in the `individuals` vector of its `Subpopulation`.

`migrant => (logical$)`

Set to `T` if the individual migrated during the current generation, `F` otherwise.

In WF models, this flag is set at the point when a new child is generated if it is a migrant (i.e., if its source subpopulation is not the same as its subpopulation), and remains valid, with the same value, for the rest of the individual's lifetime.

In nonWF models, this flag is `F` for all new individuals, is set to `F` in all individuals at the end of the reproduction generation cycle stage, and is set to `T` on all individuals moved to a new subpopulation by `takeMigrants()`; the `T` value set by `takeMigrants()` will remain until it is reset at the end of the next reproduction generation cycle stage.

`pedigreeID => (integer$)`

If pedigree tracking is turned on with `initializeSLiMOptions(keepPedigrees=T)`, `pedigreeID` is a unique non-negative identifier for each individual in a simulation, never re-used throughout the duration of the simulation run. If pedigree tracking is not on, the value of `pedigreeID` will be a singleton `-1`.

`pedigreeParentIDs => (integer)`

If pedigree tracking is turned on with `initializeSLiMOptions(keepPedigrees=T)`, `pedigreeParentIDs` contains the values of `pedigreeID` that were possessed by the parents of an individual; it is thus a vector of two values. If pedigree tracking is not on, `pedigreeParentIDs` will contain two `-1` values. Parental values may also be `-1` if insufficient generations have elapsed for that information to be available (because the simulation just started, or because a subpopulation is new).

`pedigreeGrandparentIDs => (integer)`

If pedigree tracking is turned on with `initializeSLiMOptions(keepPedigrees=T)`, `pedigreeGrandparentIDs` contains the values of `pedigreeID` that were possessed by the grandparents of an individual; it is thus a vector of four values. If pedigree tracking is not on, `pedigreeGrandparentIDs` will contain four `-1` values. Grandparental values may also be `-1` if insufficient generations have elapsed for that information to be available (because the simulation just started, or because a subpopulation is new).

`sex => (string$)`

The sex of the individual. This will be `"H"` if sex is not enabled in the simulation (i.e., for hermaphrodites), otherwise `"F"` or `"M"` as appropriate.

`spatialPosition => (float)`

The spatial position of the individual. The length of the `spatialPosition` property (the number of coordinates in the spatial position of an individual) depends upon the spatial dimensionality declared with `initializeSLiMOptions()`. If the spatial dimensionality is zero (as it is by default), it is an error to access this property. The elements of this property are identical to the values of the `x`, `y`, and `z` properties (if those properties are encompassed by the spatial dimensionality of the simulation). In other words, if the declared dimensionality is `"xy"`, the `individual.spatialPosition` property is equivalent to `c(individual.x, individual.y)`; `individual.z` is not used since it is not encompassed by the simulation's dimensionality. This property cannot be set, but the `setSpatialPosition()` method may be used to achieve the same thing.

`subpopulation => (object<Subpopulation>$)`

The `Subpopulation` object to which the individual belongs.

`tag <–> (integer$)`

A user-defined `integer` value (as opposed to `tagF`, which is of type `float`). The value of `tag` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code. The value of `tag` is not used by SLiM; it is free for you to use. See also the `getValue()` and `setValue()` methods, for another way of attaching state to individuals.

Note that the `Individual` objects used by SLiM are (conceptually) new with every generation, so the `tag` value of each new offspring generated in each generation will be initially undefined. If you set a `tag` value for an offspring individual inside a `modifyChild()` callback, that `tag` value will be preserved as the offspring individual becomes a parent (across the generation boundary, in other words). If you take advantage of this, however, you should be careful to set up initial values for the tag values of *all* offspring, otherwise undefined initial values might happen to match the values that you are trying to use to tag particular individuals. A rule of thumb in programming: undefined values should always be assumed to take on the most inconvenient value possible.

`tagF <–> (float$)`

A user-defined `float` value (as opposed to `tag`, which is of type `integer`). The value of `tagF` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code. The value of `tagF` is not used by SLiM; it is free for you to use. See also the `getValue()` and `setValue()` methods, for another way of attaching state to individuals.

Note that at present, although many classes in SLiM have an `integer`-type `tag` property, only `Individual` has a `float`-type `tagF` property, because attaching model state to individuals seems to be particularly common and useful. If a `tagF` property would be helpful on another class, it would be easy to add.

See the description of the `tag` property above for additional comments.

`uniqueMutations => (object<Mutation>)`

All of the `Mutation` objects present in this individual. Mutations present in both genomes will occur only once in this property, and the mutations will be given in sorted order by `position`, so this property is similar to `sortBy(unique(individual.genomes.mutations), "position")`. It is not identical to that call, only because if multiple mutations exist at the exact same position, they may be sorted differently by this method than they would be by `sortBy()`. This method is provided primarily for speed; it executes much faster than the Eidos equivalent above. Indeed, it is faster than just `individual.genomes.mutations`, and gives uniquing and sorting on top of that, so it is advantageous unless duplicate entries for homozygous mutations are actually needed.

`x <–> (float$)`

A user-defined `float` value. The value of `x` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code, typically in a `modifyChild()` callback. The value of `x` is not used by SLiM unless the optional "continuous space" facility is enabled with the `dimensionality` parameter to `initializeSLiMOptions()`, in which case `x` will be understood to represent the *x* coordinate of the individual in space. If continuous space is not enabled, you may use `x` as an additional tag value of type `float`.

`y <–> (float$)`

A user-defined `float` value. The value of `y` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code, typically in a `modifyChild()` callback. The value of `y` is not used by SLiM unless the optional "continuous space" facility is enabled with the `dimensionality` parameter to `initializeSLiMOptions()`, in which case `y` will be understood to represent the *y* coordinate of the individual in space (if the dimensionality is `"xy"` or `"xyz"`). If continuous space is not enabled, or the dimensionality is not `"xy"` or `"xyz"`, you may use `y` as an additional tag value of type `float`.

`z <–> (float$)`

A user-defined `float` value. The value of `z` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code, typically in a `modifyChild()` callback. The value of `z` is not used by SLiM unless the optional "continuous space" facility is enabled with the `dimensionality` parameter to `initializeSLiMOptions()`, in which case `z` will be understood to represent the *z* coordinate of the individual in space (if the dimensionality is `"xyz"`). If continuous space is not enabled, or the dimensionality is not `"xyz"`, you may use `z` as an additional tag value of type `float`.

21.6.2 `Individual` methods

`– (logical)containsMutations(object<Mutation> mutations)`

Returns a `logical` vector indicating whether each of the mutations in `mutations` is present in the individual (in either of its genomes); each element in the returned vector indicates whether the corresponding mutation is present (`T`) or absent (`F`). This method is provided for speed; it is much faster than the corresponding Eidos code.

`– (integer$)countOfMutationsOfType(io<MutationType>$ mutType)`

Returns the number of mutations that are of the type specified by `mutType`, out of all of the mutations in the individual (in both of its genomes; a mutation that is present in both genomes counts twice). If you need a vector of the matching `Mutation` objects, rather than just a count, you should probably use `uniqueMutationsOfType()`. This method is provided for speed; it is much faster than the corresponding Eidos code.

`– (+)getValue(string$ key)`

Returns the value previously set for the dictionary entry identifier `key` using `setValue()`, or `NULL` if no value has been set. This dictionary-style functionality is actually provided by the superclass of `Individual`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

`– (float)relatedness(object<Individual> individuals)`

Returns a vector containing the degrees of relatedness between the receiver and each of the individuals in `individuals`. The relatedness between `A` and `B` is always `1.0` if `A` and `B` are actually the same individual; this facility works even if SLiM's optional pedigree tracking is turned off (in which case all other relatedness values will be `0.0`). Otherwise, if pedigree tracking is turned on with `initializeSLiMOptions(keepPedigrees=T)`, this method will use the pedigree information described in section 21.6.1 to construct a relatedness estimate. More specifically, if information about the grandparental generation is available, then each grandparent shared by `A` and `B` contributes `0.125` towards the total relatedness, for a maximum value of `0.5` with four shared grandparents. If grandparental information in unavailable, then if parental information is available it is used, with each parent shared by `A` and `B` contributing `0.25`, again for a maximum of `0.5`. If even parental information is unavailable, then the relatedness is assumed to be `0.0`. Again, however, if `A` and `B` are the same individual, the relatedness will be `1.0` in all cases.

Note that this relatedness is simply pedigree-based relatedness. This does not necessarily correspond to genetic relatedness, because of the effects of factors like assortment and recombination.

`+ (void)setSpatialPosition(float position)`

Sets the spatial position of the individual (as accessed through the `spatialPosition` property). The length of `position` (the number of coordinates in the spatial position of an individual) depends upon the spatial dimensionality declared with `initializeSLiMOptions()`. If the spatial dimensionality is zero (as it is by default), it is an error to call this method. The elements of `position` are set into the values of the `x`, `y`, and `z` properties (if those properties are encompassed by the spatial dimensionality of the simulation). In other words, if the declared dimensionality is `"xy"`, calling `individual.setSpatialPosition(c(1.0, 0.5))` property is equivalent to `individual.x = 1.0; individual.y = 0.5`; `individual.z` is not set (even if a third value is supplied in `position`) since it is not encompassed by the simulation's dimensionality in this example.

Note that this is an Eidos class method, somewhat unusually, which allows it to work in a special way when called on a vector of individuals. When the target vector of individuals is non-singleton, this method can do one of two things. If `position` contains just a single point (i.e., is equal in length to the spatial dimensionality of the model), the spatial position of all of the target individuals will be set to the given point. Alternatively, if `position` contains one point per target individual (i.e., is equal in length to the number of individuals multiplied by the spatial dimensionality of the model), the spatial position of each target individual will be set to the corresponding point from `position` (where the point data is concatenated, not interleaved, just as it would be returned by accessing the `spatialPosition` property on the vector of target individuals). Calling this method with a `position` vector of any other length is an error.

`– (void)setValue(string$ key, + value)`

Sets a value for the dictionary entry identifier `key`. The value, which may be of any type other than `object`, can be fetched later using `getValue()`. This dictionary-style functionality is actually provided by the superclass of `Individual`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

`– (float$)sumOfMutationsOfType(io<MutationType>$ mutType)`

Returns the sum of the selection coefficients of all mutations that are of the type specified by `mutType`, out of all of the mutations in the genomes of the individual. This is often useful in models that use a particular mutation type to represent QTLs with additive effects; in that context, `sumOfMutationsOfType()` will provide the sum of the additive effects of the QTLs for the given mutation type. This method is provided for speed; it is much faster than the corresponding Eidos code. Note that this method also exists on `Genome`, for cases in which the sum for just one genome is desired.

`– (object<Mutation>)uniqueMutationsOfType(io<MutationType>$ mutType)`

Returns an `object` vector of all the mutations that are of the type specified by `mutType`, out of all of the mutations in the individual. Mutations present in both genomes will occur only once in the result of this method, and the mutations will be given in sorted order by `position`, so this method is similar to `sortBy(unique(individual.genomes.mutationsOfType(mutType)), "position")`. It is not identical to that call, only because if multiple mutations exist at the exact same position, they may be sorted differently by this method than they would be by `sortBy()`. If you just need a count of the matching `Mutation` objects, rather than a vector of the matches, use `–countOfMutationsOfType()`. This method is provided for speed; it is much faster than the corresponding Eidos code. Indeed, it is faster than just `individual.genomes.mutationsOfType(mutType)`, and gives uniquing and sorting on top of that, so it is advantageous unless duplicate entries for homozygous mutations are actually needed.

21.7 Class InteractionType

This class represents a type of interaction between individuals. This is an advanced feature, the use of which is optional. Once an interaction type is set up with `initializeInteractionType()` (see section 21.1), it can be evaluated and then queried to give information such as the nearest interacting neighbor of an individual, or the total strength of interactions felt by an individual, relatively efficiently. Interactions are often spatial, depending upon the spatial dimensionality established with `initializeSLiMOptions()` (section 21.1), but do not need to be spatial. Spatial interactions can have – and almost always should have – a maximum distance, which allows them to be evaluated more efficiently (since all interactions beyond the maximum distance can be assumed to have a strength of zero).

Note that if there are *N* individuals in a given subpopulation, each of which interacts with *M* other individuals, then InteractionType's internal data structures will occupy an amount of memory roughly proportional to $N \times M$, for each evaluated subpopulation. Depending upon the queries executed, interactions may also take computational time proportional to $N \times M$, or even proportional to N^2, in each evaluated subpopulation. Modeling interactions with large population sizes can therefore be expensive, although InteractionType goes to considerable lengths to minimize the overhead.

The first step in InteractionType's evaluation of an interaction is to determine the distance from the individual receiving the interaction to the individual exerting the interaction. This is computed as the Euclidean distance between the spatial positions of the individuals, based upon the spatiality of the interaction (i.e., the spatial dimensions used by the interaction, which may be less than the dimensionality of the simulation as a whole). Second, this distance is compared to the maximum distance for the interaction type; if it is beyond that limit, the interaction strength is always zero (and it is also always zero for the interaction of an individual with itself). Third (when the distance is less than the maximum), the distance is converted into an interaction strength by an interaction function (IF), which is a characteristic of the InteractionType. Finally, this interaction strength may be modified by the `interaction()` callbacks currently active in the simulation, if any (see section 22.6).

`InteractionType` is actually a wrapper for three different spatial query engines that share some of their data but work very differently. The first engine is a brute-force engine that simply computes distances and interaction strengths in response to queries. This engine is usually used in response to queries for simple information, such as the `distance()`, `distanceToPoint()`, and `strength()` methods.

The second engine is based upon a data structure called a "*k*-d tree" that is designed to optimize searches for spatially proximate points. This engine is usually used in response to queries involving "neighbors", such as `nearestNeighbors()` and `nearestNeighborsOfPoint()`. In SLiM, the term "neighbor" means an individual that is within the maximum interaction distance of a focal individual or point (excluding the focal individual itself); the neighbors of the focal individual or point are therefore those that fall within the fixed radius defined by the maximum interaction distance. Calls with "neighbor" in their name explicitly use the *k*-d tree engine, and may therefore be called only for spatial interactions; in non-spatial interactions there is no concept of a "neighbor". In terms of computational complexity, finding the nearest neighbor of a given individual using the brute-force engine is an O(*N*) computation, whereas with the *k*-d tree engine it is typically an O(log *N*) computation – a very important difference, especially for large *N*. In general, to get the best performance from a spatial model, you should (1) set a maximum distance for the model interactions that is as small as possible without introducing unwanted artifacts, and (2) use neighbor-based calls to make minimal queries when possible – if all you really care about is the distance to the nearest neighbor, use `nearestNeighbors()` to find the neighbor and then call `distance()` to get the distance to that neighbor, rather than getting the distances to all individuals with `distance()` and then using `min()` to select the smallest, for example.

The third engine, introduced in SLiM 3.1, is based upon a data structure called a "sparse array" that is designed to track sparse non-zero values within a dataset that contains mostly zeros. It applies to spatial interactions because most pairs of interactions probably interact with a strength of zero (because typically $N >> M$, because few individuals fall within the maximum interaction radius from a given individual). The sparse array is used to cache all calculated distance/strength pairs for interactions within a given subpopulation. It is built using the *k*-d tree to find the interacting neighbors of each individual, and once built it can respond extremely quickly to queries from methods such as `totalOfNeighborStrengths()`; the interacting neighbors of a given individual are already known, allowing response in $O(M)$ time. The sparse array is built on demand, when queries that would benefit from it are made. For it to be effective, it is particularly important that a maximum interaction distance be used that is as small as possible, so beginning with SLiM 3.1 a warning is issued when no maximum distance is defined for spatial interactions.

There are currently four options for interaction functions (IFs) in SLiM, represented by single-character codes:

`"f"` – a **f**ixed interaction strength. This IF type has a single parameter, the interaction strength to be used for all interactions of this type. By default, interaction types use a type `"f"` IF with a value of 1.0, so interactions are binary: on within the maximum distance, off outside.

`"l"` – a **l**inear interaction strength. This IF type has a single parameter, the maximum interaction strength to be used at distance `0.0`. The interaction strength falls off linearly, reaching exactly zero at the maximum distance. In other words, for distance d, maximum interaction distance $d_{\max}$, and maximum interaction strength $f_{\max}$, the formula for this IF is $f(d) = f_{\max}(1 - d / d_{\max})$.

`"e"` – A negative **e**xponential interaction strength. This IF type is specified by two parameters, a maximum interaction strength and a shape parameter. The interaction strength falls off non-linearly from the maximum, and cuts off discontinuously at the maximum distance; typically a maximum distance is chosen such that the interaction strength at that distance is very small anyway. The IF for this type is $f(d) = f_{\max}\exp(-\lambda d)$, where λ is the specified shape parameter. Note that this parameterization is *not* the same as for the Eidos function `rexp()`.

`"n"` – A **n**ormal interaction strength (i.e., Gaussian, but `"g"` is avoided to prevent confusion with the gamma-function option provided for, e.g., `MutationType`). The interaction strength falls off non-linearly from the maximum, and cuts off discontinuously at the maximum distance; typically a maximum distance is chosen such that the interaction strength at that distance is very small anyway. This IF type is specified by two parameters, a maximum interaction strength and a standard deviation. The Gaussian IF for this type is $f(d) = f_{\max}\exp(-d^2/2\sigma^2)$, where σ is the standard deviation parameter. Note that this parameterization is *not* the same as for the Eidos function `rnorm()`. A Gaussian function is often used to model spatial interactions, but is relatively computation-intensive.

`"c"` – A **C**auchy-distributed interaction strength. The interaction strength falls off non-linearly from the maximum, and cuts off discontinuously at the maximum distance; typically a maximum distance is chosen such that the interaction strength at that distance is very small anyway. This IF type is specified by two parameters, a maximum interaction strength and a scale parameter. The IF for this type is $f(d) = f_{\max}/(1+(d/\lambda)^2)$, where λ is the scale parameter. Note that this parameterization is *not* the same as for the Eidos function `rcauchy()`. A Cauchy distribution can be used to model interactions with relatively fat tails.

An `InteractionType` may be allocated using the `initializeInteractionType()` function (see section 21.1). It must then be evaluated, with the `evaluate()` method, for any given subpopulation before it will respond to queries regarding that subpopulation. This causes the positions of all individuals to be cached, thus defining a snapshot in time that the `InteractionType` will then use to respond to queries (necessary since the positions of individuals may change at any time). This evaluated state will last until the current parental generation expires, at the end of the next offspring-generation phase. Before the `InteractionType` may be used with the new parental generation (the offspring of the old parental generation), the interaction must be evaluated again.

`InteractionType` will automatically account for any periodic spatial boundaries established with the `periodicity` parameter of `initializeSLiMOptions()`; interactions will wrap around the periodic boundaries without any additional configuration of the interaction. Interactions involving periodic spatial boundaries entail some additional overhead in both memory usage and processor time; in particular, setting up the *k*-d tree after the interaction is evaluated may take many times longer than in the non-periodic case. Once the *k*-d tree has been set up, however, responses to spatial queries involving it should then be nearly as fast as in the non-periodic case. Spatial queries that do not involve the *k*-d tree will generally be marginally slower than in the non-periodic case, but the difference should not be large.

21.7.1 `InteractionType` properties

`id => (integer$)`

The identifier for this interaction type; for interaction type `i3`, for example, this is `3`.

`maxDistance <–> (float$)`

The maximum distance over which this interaction will be evaluated. For inter-individual distances greater than `maxDistance`, the interaction strength will be zero.

`reciprocal => (logical$)`

The reciprocality of the interaction, as specified in `initializeInteractionType()`. This will be `T` for reciprocal interactions (those for which the interaction strength of B upon A is equal to the interaction strength of A upon B), and `F` otherwise.

`sexSegregation => (string$)`

The sex-segregation of the interaction, as specified in `initializeInteractionType()`. For non-sexual simulations, this will be `"**"`. For sexual simulations, this `string` value indicates the sex of individuals feeling the interaction, and the sex of individuals exerting the interaction; see `initializeInteractionType()` for details.

`spatiality => (string$)`

The spatial dimensions used by the interaction, as specified in `initializeInteractionType()`. This will be `""` (the empty string) for non-spatial interactions, or `"x"`, `"y"`, `"z"`, `"xy"`, `"xz"`, `"yz"`, or `"xyz"`, for interactions using those spatial dimensions respectively. The specified dimensions are used to calculate the distances between individuals for this interaction. The value of this property is always the same as the value given to `initializeInteractionType()`.

`tag <–> (integer$)`

A user-defined `integer` value. The value of `tag` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code. The value of `tag` is not used by SLiM; it is free for you to use. See also the `getValue()` and `setValue()` methods, for another way of attaching state to interaction types.

21.7.2 *`InteractionType` methods*

– `(float)distance(object<Individual> individuals1, [No<Individual> individuals2 = NULL])`

Returns a vector containing distances between individuals in `individuals1` and `individuals2`. At least one of `individuals1` or `individuals2` must be singleton, so that the distances evaluated are either from one individual to many, or from many to one (which are equivalent, in fact); evaluating distances for many to many individuals cannot be done in a single call. (There is one exception: if both `individuals1` and `individuals2` are zero-length or `NULL`, a zero-length float vector will be returned.) If `individuals2` is `NULL` (the default), then `individuals1` must be singleton, and a vector of the distances from that individual to all individuals in its subpopulation (including itself) is returned; this case may be handled differently internally, for greater speed, so supplying `NULL` is preferable to supplying the vector of all individuals in the subpopulation explicitly even though that should produce identical results. If the `InteractionType` is non-spatial, this method may not be called.

Importantly, distances are calculated according to the spatiality of the `InteractionType` (as declared in `initializeInteractionType()`), not the dimensionality of the model as a whole (as declared in `initializeSLiMOptions()`). The distances returned are therefore the distances that would be used to calculate interaction strengths. However, `distance()` will return finite distances for all pairs of individuals, even if the individuals are non-interacting; the `distance()` between an individual and itself will thus be `0`. See `interactionDistance()` for an alternative distance definition.

– `(float)distanceToPoint(object<Individual> individuals1, float point)`

Returns a vector containing distances between individuals in `individuals1` and the point given by the spatial coordinates in `point`. The `point` vector is interpreted as providing coordinates precisely as specified by the spatiality of the interaction type; if the interaction type's spatiality is `"xz"`, for example, then `point[0]` is assumed to be an *x* value, and `point[1]` is assumed to be a *z* value. Be careful; this means that in general it is not safe to pass an individual's `spatialPosition` property for `point`, for example (although it is safe if the spatiality of the interaction matches the dimensionality of the simulation). A coordinate for a periodic spatial dimension must be within the spatial bounds for that dimension, since coordinates outside of periodic bounds are meaningless (`pointPeriodic()` may be used to ensure this); coordinates for non-periodic spatial dimensions are not restricted.

Importantly, distances are calculated according to the spatiality of the `InteractionType` (as declared in `initializeInteractionType()`) not the dimensionality of the model as a whole (as declared in `initializeSLiMOptions()`). The distances are therefore interaction distances: the distances that are used to calculate interaction strengths. If the `InteractionType` is non-spatial, this method may not be called. The vector `point` must be exactly as long as the spatiality of the `InteractionType`.

– `(object<Individual>)drawByStrength(object<Individual>$ individual, [integer$ count = 1])`

Returns up to `count` individuals drawn from the subpopulation of `individual`. The probability of drawing particular individuals is proportional to the strength of interaction they exert upon `individual`. This method may be used with either spatial or non-spatial interactions, but will be more efficient with spatial interactions that set a short maximum interaction distance. Draws are done with replacement, so the same individual may be drawn more than once; sometimes using `unique()` on the result of this call is therefore desirable. If more than one draw will be needed, it is much more efficient to use a single call to `drawByStrength()`, rather than drawing individuals one at a time. Note that if no individuals exert a non-zero interaction upon `individual`, the vector returned will be zero-length; it is important to consider this possibility.

If the needed interaction strengths have already been calculated, those cached values are simply used. Otherwise, calling this method triggers evaluation of the needed interactions, including calls to any applicable `interaction()` callbacks.

– `(void)evaluate([No<Subpopulation> subpops = NULL], [logical$ immediate = F])`

Triggers evaluation of the interaction for the subpopulations specified by `subpops` (or for all subpopulations, if `subpops` is `NULL`). By default, the effects of this may be limited, however, since the underlying implementation may choose to postpone some computations lazily. At a minimum, is it guaranteed that this method will discard all previously cached data for the subpopulation(s), and will cache the current positions of all individuals (so that individuals may then move without disturbing the state of the interaction at the moment of evaluation). Notably, `interaction()` callbacks may not be called in response to this method; instead, their evaluation may be deferred until required to satisfy queries (at which point the generation counter may have advanced by one, so be careful with the generation ranges used in defining such callbacks).

If `T` is passed for `immediate`, the interaction will immediately and synchronously evaluate all interactions between all individuals in the subpopulation(s), calling any applicable `interaction()` callbacks as necessary. However, depending upon what queries are later executed, this may represent considerable wasted computation, since it is an O(N^2) operation. Immediate evaluation usually generates only a slight performance improvement even if the interactions between all pairs of individuals are eventually accessed; the main reason to choose immediate evaluation, then, is that deferred calculation of interactions would lead to incorrect results due to changes in model state.

You must explicitly call `evaluate()` at an appropriate time in the life cycle before the interaction is used, but after any relevant changes have been made to the population. SLiM will invalidate any existing interactions after any portion of the generation cycle in which new individuals have been born or existing individuals have died. In a WF model, these events occur just before `late()` events execute (see the WF generation cycle diagram in chapter 19), so `late()` events are often the appropriate place to put `evaluate()` calls, but `early()` events can work too if the interaction is not needed until that point in the generation cycle anyway. In nonWF models, on the other hand, new offspring are produced just before `early()` events and then individuals die just before `late()` events (see the nonWF generation cycle diagram in chapter 20), so interactions will be invalidated twice during each generation cycle. This means that in a nonWF model, an interaction that influences reproduction should usually be evaluated in a `late()` event, while an interaction that influences fitness or mortality should usually be evaluated in an `early()` event (and an interaction that affects both may need to be evaluated at both times).

If an interaction is never evaluated for a given subpopulation, it is guaranteed that there will be essentially no memory or computational overhead associated with the interaction for that subpopulation. Furthermore, attempting to query an interaction for an individual in a subpopulation that has not been evaluated is guaranteed to raise an error.

– `(+)getValue(string$ key)`

Returns the value previously set for the dictionary entry identifier `key` using `setValue()`, or `NULL` if no value has been set. This dictionary-style functionality is actually provided by the superclass of `InteractionType`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

– `(integer)interactingNeighborCount(object<Individual> individuals)`

Returns the number of interacting individuals for each individual in `individuals`, within the maximum interaction distance according to the distance metric of the `InteractionType`. More specifically, this method counts the number of individuals which can *exert* an interaction *upon* each focal individual; it does not count individuals which only *feel* an interaction *from* a focal individual. This method is similar to `nearestInteractingNeighbors()` (when passed a large count so as to guarantee that all interacting individuals are returned), but this method returns only a count of the interacting individuals, not a vector containing the individuals. This method may also be called in a vectorized fashion, with a non-singleton vector of individuals, unlike `nearestInteractingNeighbors()`.

Note that this method uses interaction eligibility as a criterion; it will not count neighbors that cannot exert an interaction upon a focal individual (due to sex-segregation, e.g.). (It also does not count a focal individual as a neighbor of itself.)

– `(float)interactionDistance(object<Individual>$ receiver, [No<Individual> exerters = NULL])`

Returns a vector containing interaction-dependent distances between `receiver` and individuals in `exerters` that exert an interaction strength upon `receiver`. If `exerters` is `NULL` (the default), then a vector of the interaction-dependent distances from `receiver` to all individuals in its subpopulation (including `receiver` itself) is returned; this case may be handled much more efficiently than if a vector of all individuals in the subpopulation is explicitly provided. If the `InteractionType` is non-spatial, this method may not be called.

Importantly, distances are calculated according to the spatiality of the `InteractionType` (as declared in `initializeInteractionType()`), not the dimensionality of the model as a whole (as declared in `initializeSLiMOptions()`). The distances returned are therefore the distances that would be used to calculate interaction strengths. In addition, `interactionDistance()` will return `INF` as the distance between `receiver` and any individual which does not exert an interaction upon `receiver`; the `interactionDistance()` between an individual and itself will thus be `INF`, and likewise for pairs excluded from interacting by the sex segregation or max distance of the interaction type. See `distance()` for an alternative distance definition.

– `(object<Individual>)nearestInteractingNeighbors(object<Individual>$ individual, [integer$ count = 1])`

Returns up to `count` interacting individuals that are spatially closest to `individual`, according to the distance metric of the `InteractionType`. More specifically, this method returns only individuals which can *exert* an interaction *upon* the focal individual; it does not include individuals that only *feel* an interaction *from* the focal individual. To obtain all of the interacting individuals within the maximum interaction distance of `individual`, simply pass a value for `count` that is greater than or equal to the size of `individual`'s subpopulation. Note that if fewer than `count` interacting individuals are within the maximum interaction distance, the vector returned may be shorter than `count`, or even zero-length; it is important to check for this possibility even when requesting a single neighbor. If only the number of interacting individuals is needed, use `interactingNeighborCount()` instead.

Note that this method uses interaction eligibility as a criterion; it will not return neighbors that cannot exert an interaction upon the focal individual (due to sex-segregation, e.g.). (It will also never return the focal individual as a neighbor of itself.) To find all neighbors of the focal individual, whether they can interact with it or not, use `nearestNeighbors()`.

– `(object<Individual>)nearestNeighbors(object<Individual>$ individual, [integer$ count = 1])`

Returns up to `count` individuals that are spatially closest to `individual`, according to the distance metric of the `InteractionType`. To obtain all of the individuals within the maximum interaction distance of `individual`, simply pass a value for `count` that is greater than or equal to the size of `individual`'s subpopulation. Note that if fewer than `count` individuals are within the maximum interaction distance, the vector returned may be shorter than `count`, or even zero-length; it is important to check for this possibility even when requesting a single neighbor.

Note that this method does not use interaction eligibility as a criterion; it will return neighbors that could not interact with the focal individual due to sex-segregation. (It will never return the focal individual as a neighbor of itself, however.) To find only neighbors that are eligible to exert an interaction upon the focal individual, use `nearestInteractingNeighbors()`.

– `(object<Individual>)nearestNeighborsOfPoint(object<Subpopulation>$ subpop, float point, [integer$ count = 1])`

Returns up to `count` individuals in `subpop` that are spatially closest to `point`, according to the distance metric of the `InteractionType`. To obtain all of the individuals within the maximum interaction distance of `point`, simply pass a value for `count` that is greater than or equal to the size of `subpop`. Note that if fewer than `count` individuals are within the maximum interaction distance, the vector returned may be shorter than `count`, or even zero-length; it is important to check for this possibility even when requesting a single neighbor.

– `(void)setInteractionFunction(string$ functionType, ...)`

Set the function used to translate spatial distances into interaction strengths for an interaction type. The `functionType` may be `"f"`, in which case the ellipsis `...` should supply a `numeric$` fixed interaction strength; `"l"`, in which case the ellipsis should supply a `numeric$` maximum strength for a linear function; `"e"`, in which case the ellipsis should supply a `numeric$` maximum strength and a `numeric$` lambda (shape) parameter for a negative exponential function; `"n"`, in which case the ellipsis should supply a `numeric$` maximum strength and a `numeric$` sigma (standard deviation) parameter for a Gaussian function; or `"c"`, in which case the ellipsis should supply a `numeric$` maximum strength and a `numeric$` scale parameter for a Cauchy distribution function. See section 21.7 above for discussions of these interaction functions. Non-spatial interactions must use function type `"f"`, since no distance values are available in that case.

The interaction function for an interaction type is normally a constant in simulations; in any case, it cannot be changed when an interaction has already been evaluated for a given generation of individuals.

– `(void)setValue(string$ key, + value)`

Sets a value for the dictionary entry identifier `key`. The value, which may be of any type other than `object`, can be fetched later using `getValue()`. This dictionary-style functionality is actually provided by the superclass of `InteractionType`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

– `(float)strength(object<Individual>$ receiver, [No<Individual> exerters = NULL])`

Returns a vector containing the interaction strengths exerted upon `receiver` by the individuals in `exerters`. If `exerters` is `NULL` (the default), then a vector of the interaction strengths exerted by all individuals in the subpopulation of `receiver` (including `receiver` itself) is returned; this case may be handled much more efficiently than if a vector of all individuals in the subpopulation is explicitly provided.

If the strengths of interactions exerted by a single individual upon multiple individuals is needed instead (the inverse of what this method provides), multiple calls to this method will be necessary, one per pairwise interaction queried; the interaction engine is not optimized for the inverse case, and so it will likely be quite slow to compute. If the interaction is reciprocal and sex-symmetric, the opposite query should provide identical results in a single efficient call (because then the interactions exerted are equal to the interactions received); otherwise, the best approach might be to define a second interaction type representing the inverse interaction that you wish to be able to query efficiently.

If the needed interaction strengths have already been calculated, those cached values are simply returned. Otherwise, calling this method triggers evaluation of the needed interactions, including calls to any applicable `interaction()` callbacks.

– `(float)totalOfNeighborStrengths(object<Individual> individuals)`

Returns a vector of the total interaction strength felt by each individual in `individuals`, which does not need to be a singleton; indeed, it can be a vector of all of the individuals in a given subpopulation. However, all of the individuals in `individuals` must be in the same subpopulation.

For one individual, this is essentially the same as calling `nearestNeighbors()` with a large `count` so as to obtain the complete vector of all neighbors, calling `strength()` for each of those interactions to get each interaction strength, and adding those interaction strengths together with `sum()`. This method is much faster than that implementation, however, since all of that work is done as a single operation. Also, `totalOfNeighborStrengths()` can total up interactions for more than one focal individual in a single call.

Similarly, for one individual this is essentially the same as calling `strength()` to get the interaction strengths between the focal individual and all other individuals, and then calling `sum()`. Again, this method should be much faster, since this algorithm looks only at neighbors, whereas calling `strength()` directly assesses interaction strengths with all other individuals. This will make a particularly large difference when the subpopulation size is large and the maximum distance of the `InteractionType` is small.

If the needed interaction strengths have already been calculated, those cached values are simply used. Otherwise, calling this method triggers evaluation of the needed interactions, including calls to any applicable `interaction()` callbacks.

`– (void)unevaluate(void)`

Discards all evaluation of this interaction, for all subpopulations. The state of the `InteractionType` is reset to a state prior to evaluation. This can be useful if the model state has changed in such a way that the evaluation already conducted is no longer valid. For example, if the maximum distance or the interaction function of the `InteractionType` need to be changed with immediate effect, or if the data used by an interaction() callback has changed in such a way that previously calculated interaction strengths are no longer correct, `unevaluate()` allows the interaction to begin again from scratch.

Note that all interactions are automatically reset to an unevaluated state at the moment when the new offspring generation becomes the parental generation (at step 4 in the generation cycle; see section 19.4). Most simulations therefore never have any reason to call `unevaluate()`.

21.8 Class Mutation

This class represents a single point mutation. Mutations can be shared by the genomes of many individuals; if they reach fixation, they are converted to `Substitution` objects.

Although `Mutation` has a `tag` property, like most SLiM classes, the `subpopID` can also store custom values if you don't need to track the origin subpopulation of mutations (see below).

Section 1.5.2 presents an overview of the conceptual role of this class.

21.8.1 `Mutation` properties

`id => (integer$)`

The identifier for this mutation. Each mutation created during a run receives an immutable identifier that will be unique across the duration of the run. These identifiers are not re-used during a run, except that if a population file is loaded from disk, the loaded mutations will receive their original identifier values as saved in the population file.

`mutationType => (object<MutationType>$)`

The `MutationType` from which this mutation was drawn.

`originGeneration => (integer$)`

The generation in which this mutation arose.

`position => (integer$)`

The position in the chromosome of this mutation.

`selectionCoeff => (float$)`

The selection coefficient of the mutation, drawn from the distribution of fitness effects of its `MutationType`. If a mutation has a `selectionCoeff` of *s*, the multiplicative fitness effect of the mutation in a homozygote is 1+*s*; in a heterozygote it is 1+*hs*, where *h* is the dominance coefficient kept by the mutation type (see section 21.9.1).

Note that this property has a quirk: it is stored internally in SLiM using a single-precision float, not the double-precision float type normally used by Eidos. This means that if you set a mutation `mut`'s selection coefficient to some number `x`, `mut.selectionCoeff==x` may be `F` due to floating-point rounding error. Comparisons of floating-point numbers for exact equality is often a bad idea, but this is one case where it may fail unexpectedly. Instead, it is recommended to use the `id` or `tag` properties to identify particular mutations.

`subpopID <–> (integer$)`

The identifier of the subpopulation in which this mutation arose. This property can be used to track the ancestry of mutations through their subpopulation of origin. For an overview of other ways of tracking genetic ancestry, including true local ancestry at each position on the chromosome, see section 13.9.

If you don't care which subpopulation a mutation originated in, the `subpopID` may be used as an arbitrary `integer` "tag" value for any purpose you wish; SLiM does not do anything with the value of `subpopID` except propagate it to `Substitution` objects and report it in output. (It must still be `>= 0`, however, since SLiM object identifiers are limited to nonnegative integers).

`tag <–> (integer$)`

A user-defined `integer` value. The value of `tag` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code. The value of `tag` is not used by SLiM; it is free for you to use.

21.8.2 `Mutation` methods

`– (+)getValue(string$ key)`

Returns the value previously set for the dictionary entry identifier `key` using `setValue()`, or `NULL` if no value has been set. This dictionary-style functionality is actually provided by the superclass of `Mutation`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

`– (void)setMutationType(io<MutationType>$ mutType)`

Set the mutation type of the mutation to `mutType` (which may be specified as either an `integer` identifier or a `MutationType` object). This implicitly changes the dominance coefficient of the mutation to that of the new mutation type, since the dominance coefficient is a property of the mutation type. On the other hand, the selection coefficient of the mutation is not changed, since it is a property of the mutation object itself; it can be changed explicitly using the `setSelectionCoeff()` method if so desired.

The mutation type of a mutation is normally a constant in simulations, so be sure you know what you are doing. Changing this will normally affect the fitness values calculated at the end of the current generation; if you want current fitness values to be affected, you can call `SLiMSim`'s method `recalculateFitness()` – but see the documentation of that method for caveats.

`– (void)setSelectionCoeff(float$ selectionCoeff)`

Set the selection coefficient of the mutation to `selectionCoeff`. The selection coefficient will be changed for all individuals that possess the mutation, since they all share a single `Mutation` object (note that the dominance coefficient will remain unchanged, as it is determined by the mutation type).

This is normally a constant in simulations, so be sure you know what you are doing; often setting up a `fitness()` callback (see section 22.2) is preferable, in order to modify the selection coefficient in a more limited and controlled fashion (see section 9.5 for further discussion of this point). Changing this will normally affect the fitness values calculated at the end of the current generation; if you want current fitness values to be affected, you can call `SLiMSim`'s method `recalculateFitness()` – but see the documentation of that method for caveats.

– `(void)setValue(string$ key, + value)`

Sets a value for the dictionary entry identifier `key`. The value, which may be of any type other than `object`, can be fetched later using `getValue()`. This dictionary-style functionality is actually provided by the superclass of `Mutation`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

21.9 Class MutationType

This class represents a type of mutation with a particular distribution of fitness effects, such as neutral mutations or weakly beneficial mutations. Sections 1.5.3 and 1.5.4 present an overview of the conceptual role of this class. The mutation types currently defined in the simulation are defined as global constants with the same names used in the SLiM input file – `m1`, `m2`, and so forth.

There are currently six options for the distribution of fitness effects in SLiM, represented by single-character codes:

`"f"` – A **f**ixed fitness effect. This DFE type has a single parameter, the selection coefficient s to be used by all mutations of the mutation type.

`"g"` – A **g**amma-distributed fitness effect. This DFE type is specified by two parameters, a shape parameter and a mean value. The gamma distribution from which mutations are drawn is given by the probability density function $P(s \mid \alpha,\beta) = [\Gamma(\alpha)\beta^{\alpha}]^{-1}s^{\alpha-1}\exp(-s/\beta)$, where α is the shape parameter, and the specified mean for the distribution is equal to $\alpha\beta$. Note that this parameterization is the same as for the Eidos function `rgamma()`. A gamma distribution is often used to model deleterious mutations at functional sites.

`"e"` – An **e**xponentially-distributed fitness effect. This DFE type is specified by a single parameter, the mean of the distribution. The exponential distribution from which mutations are drawn is given by the probability density function $P(s \mid \beta) = \beta^{-1}\exp(-s/\beta)$, where β is the specified mean for the distribution. This parameterization is the same as for the Eidos function `rexp()`. An exponential distribution is often used to model beneficial mutations.

`"n"` – A **n**ormally-distributed fitness effect. This DFE type is specified by two parameters, a mean and a standard deviation. The normal distribution from which mutations are drawn is given by the probability density function $P(s \mid \mu,\sigma) = (2\pi\sigma^2)^{-1/2}\exp(-(s-\mu)^2/2\sigma^2)$, where μ is the mean and σ is the standard deviation. This parameterization is the same as for the Eidos function `rnorm()`. A normal distribution is often used to model mutations that can be either beneficial or deleterious, since both tails of the distribution are unbounded.

`"w"` – A **W**eibull-distributed fitness effect. This DFE type is specified by a scale parameter and a shape parameter. The Weibull distribution from which mutations are drawn is given by the probability density function $P(s \mid \lambda,k) = (k/\lambda^k)s^{k-1}\exp(-(s/\lambda)^k)$, where λ is the scale parameter and k is the shape parameter. This parameterization is the same as for the Eidos function `rweibull()`. A Weibull distribution is often used to model mutations following extreme-value theory.

`"s"` – A **s**cript-based fitness effect. This DFE type is specified by a script parameter of type `string`, specifying an Eidos script to be executed to produce each new selection coefficient. For example, the script `"return rbinom(1);"` could be used to generate selection coefficients drawn from a binomial distribution, using the Eidos function `rbinom()`, even though that mutational distribution is not supported by SLiM directly. The script must return a singleton float or integer.

Note that these distributions can in principle produce selection coefficients smaller than `-1.0`. In that case, the mutations will be evaluated as "lethal" by SLiM, and the relative fitness of the individual will be set to `0.0`.

21.9.1 `MutationType` properties

`color <–> (string$)`

The color used to display mutations of this type in SLiMgui. Outside of SLiMgui, this property still exists, but is not used by SLiM. Colors may be specified by name, or with hexadecimal RGB values of the form `"#RRGGBB"` (see the Eidos manual). If `color` is the empty string, `""`, SLiMgui's default (selection-coefficient–based) color scheme is used; this is the default for new `MutationType` objects.

`colorSubstitution <–> (string$)`

The color used to display substitutions of this type in SLiMgui (see the discussion for the `colorSubstitution` property of the `Chromosome` class for details). Outside of SLiMgui, this property still exists, but is not used by SLiM. Colors may be specified by name, or with hexadecimal RGB values of the form `"#RRGGBB"` (see the Eidos manual). If `colorSubstitution` is the empty string, `""`, SLiMgui's default (selection-coefficient–based) color scheme is used; this is the default for new `MutationType` objects.

`convertToSubstitution <–> (logical$)`

This property governs whether mutations of this mutation type will be converted to `Substitution` objects when they reach fixation.

In WF models this property is `T` by default, since conversion to `Substitution` objects provides large speed benefits; it should be set to `F` only if necessary, and only on the mutation types for which it is necessary. This might be needed, for example, if you are using a `fitness()` callback to implement an epistatic relationship between mutations; a mutation epistatically influencing the fitness of other mutations through a `fitness()` callback would need to continue having that influence even after reaching fixation, but if the simulation were to replace the fixed mutation with a `Substitution` object the mutation would no longer be considered in fitness calculations (unless the callback explicitly consulted the list of `Substitution` objects kept by the simulation). Other script-defined behaviors in `fitness()`, `interaction()`, `mateChoice()`, `modifyChild()`, and `recombination()` callbacks might also necessitate the disabling of substitution for a given mutation type; this is an important consideration to keep in mind. See section 19.3 for further discussion of `convertToSubstitution` in WF models.

In contrast, for nonWF models this property is `F` by default, because even mutations with no epistatis or other indirect fitness effects will continue to influence the survival probabilities of individuals. For nonWF models, only neutral mutation types with no epistasis or other side effects can safely be converted to substitutions upon fixation. When such a pure-neutral mutation type is defined in a nonWF model, this property should be set to `T` to tell SLiM that substitution is allowed; this may have very large positive effects on performance, so it is important to remember when modeling background neutral mutations. See section 20.5 for further discussion of `convertToSubstitution` in nonWF models.

SLiM consults this flag at the end of each generation when deciding whether to substitute each fixed mutation. If this flag is `T`, all eligible fixed mutations will be converted at the end of the current generation, even if they were previously left unconverted because of the previous value of the flag. Setting this flag to `F` will prevent future substitutions, but will not cause any existing `Substitution` objects to be converted back into `Mutation` objects.

`distributionParams => (float)`

The parameters that configure the chosen distribution of fitness effects. This will be of type `string` for DFE type `"s"`, and type `float` for all other DFE types.

`distributionType => (string$)`

The type of distribution of fitness effects; one of `"f"`, `"g"`, `"e"`, `"n"`, `"w"`, or `"s"` (see section 21.9, above).

`dominanceCoeff <–> (float$)`

The dominance coefficient used for mutations of this type when heterozygous. Changing this will normally affect the fitness values calculated at the end of the current generation; if you want current fitness values to be affected, you can call `SLiMSim`'s method `recalculateFitness()` – but see the documentation of that method for caveats.

Note that the dominance coefficient is not bounded. A dominance coefficient greater than `1.0` may be used to achieve an overdominance effect. By making the selection coefficient very small and the dominance coefficient very large, an overdominance scenario in which both homozygotes have the same fitness may be approximated, to a nearly arbitrary degree of precision.

Note that this property has a quirk: it is stored internally in SLiM using a single-precision float, not the double-precision float type normally used by Eidos. This means that if you set a mutation type `muttype`'s dominance coefficient to some number `x`, `muttype.dominanceCoeff==x` may be `F` due to floating-point rounding error. Comparisons of floating-point numbers for exact equality is often a bad idea, but this is one case where it may fail unexpectedly. Instead, it is recommended to use the `id` or `tag` properties to identify particular mutation types.

`id => (integer$)`

The identifier for this mutation type; for mutation type `m3`, for example, this is `3`.

`mutationStackGroup <–> (integer$)`

The group into which this mutation type belongs for purposes of mutation stacking policy. This is equal to the mutation type's `id` by default. See `mutationStackPolicy`, below, for discussion.

`mutationStackPolicy <–> (string$)`

This property and the `mutationStackGroup` property together govern whether mutations of this mutation type's stacking group can "stack" – can occupy the same position in a single individual. A set of mutation types with the same value for `mutationStackGroup` is called a "stacking group", and all mutation types in a given stacking group must have the same `mutationStackPolicy` value, which defines the stacking behavior of all mutations of the mutation types in the stacking group. In other words, one stacking group might allow its mutations to stack, while another stacking group might not, but the policy within each stacking group must be unambiguous.

This property is `"s"` by default, indicating that mutations in this stacking group should be allowed to stack without restriction. If the policy is set to `"f"`, the *first* mutation of stacking group at a given site is retained; further mutations of this stacking group at the same site are discarded with no effect. This can be useful for modeling one-way changes to single nucleotides, for example; once a `T` changes to an `A`, further changes of the `A` to an `A` are not changes at all. If the policy is set to `"l"`, the *last* mutation of this stacking group at a given site is retained; earlier mutation of this stacking group at the same site are discarded. This can be useful for modeling an "infinite-alleles" scenario in which every new mutation at a site generates a completely new allele, rather than retaining the previous mutations at the site.

The mutation stacking policy applies only within the given mutation type's stacking group; mutations of different stacking groups are always allowed to stack in SLiM. The policy applies to all mutations added to the model after the policy is set, whether those mutations are introduced by calls such as `addMutation()`, `addNewMutation()`, or `addNewDrawnMutation()`, or are added by SLiM's own mutation-generation machinery. However, no attempt is made to enforce the policy for mutations already existing at the time the policy is set; typically, therefore, the policy is set in an `initialize()` callback so that it applies throughout the simulation. The policy is also not enforced upon the mutations loaded from a file with `readFromPopulationFile()`; such mutations were governed by whatever stacking policy was in effect when the population file was generated.

`tag <–> (integer$)`

A user-defined `integer` value. The value of `tag` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code. The value of `tag` is not used by SLiM; it is free for you to use. See also the `getValue()` and `setValue()` methods, for another way of attaching state to mutation types.

21.9.2 `MutationType` methods

`– (+)getValue(string$ key)`

Returns the value previously set for the dictionary entry identifier `key` using `setValue()`, or `NULL` if no value has been set. This dictionary-style functionality is actually provided by the superclass of `MutationType`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

`– (void)setDistribution(string$ distributionType, ...)`

Set the distribution of fitness effects for a mutation type. The `distributionType` may be `"f"`, in which case the ellipsis `...` should supply a `numeric$` fixed selection coefficient; `"e"`, in which case the ellipsis should supply a `numeric$` mean selection coefficient for the exponential distribution; `"g"`, in which case the ellipsis should supply a `numeric$` mean selection coefficient and a `numeric$` alpha shape parameter for a gamma distribution; `"n"`, in which case the ellipsis should supply a `numeric$` mean selection coefficient and a `numeric$` sigma (standard deviation) parameter for a normal distribution; `"w"`, in which case the ellipsis should supply a `numeric$` λ scale parameter and a `numeric$` k shape parameter for a Weibull distribution; or `"s"`, in which case the ellipsis should supply a `string$` Eidos script parameter. See section 21.9 above for discussions of these distributions and their uses. The DFE for a mutation type is normally a constant in simulations, so be sure you know what you are doing.

`– (void)setValue(string$ key, + value)`

Sets a value for the dictionary entry identifier `key`. The value, which may be of any type other than `object`, can be fetched later using `getValue()`. This dictionary-style functionality is actually provided by the superclass of `MutationType`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

21.10 Class SLiMEidosBlock

This class represents a block of Eidos code registered in a SLiM simulation. All Eidos events and Eidos callbacks defined in the SLiM input file of the current simulation are instantiated as `SLiMEidosBlock` objects and are available through the read-only `scriptBlocks` property of `SLiMSim`; see section 21.12.1. In addition, new script blocks can be created programmatically and registered with the simulation, and registered script blocks can be deregistered; see the `-register...()` and `-deregisterScriptBlock()` methods of `SLiMSim` in section 21.12.2. The currently executing script block is available through the `self` global; see section 22.8.

21.10.1 `SLiMEidosBlock` properties

`active <–> (integer$)`

If this evaluates to `logical` `F` (i.e., is equal to `0`), the script block is inactive and will not be called. The value of `active` for all registered script blocks is reset to `-1` at the beginning of each generation, prior to script events being called, thus activating all blocks. Any `integer` value other than `-1` may be used instead of `-1` to represent that a block is active; for example, `active` may be used as a counter to make a block execute a fixed number of times in each generation. This value is not cached by SLiM; if it is changed, the new value takes effect immediately. For example, a callback might be activated and inactivated repeatedly during a single generation.

`end => (integer$)`

The last generation in which the script block is active.

`id => (integer$)`

The identifier for this script block; for script `s3`, for example, this is `3`. A script block for which no `id` was given will have an `id` of `-1`.

`source => (string$)`

The source code string of the script block.

`start => (integer$)`

The first generation in which the script block is active.

`tag <–> (integer$)`

A user-defined `integer` value. The value of `tag` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code. The value of `tag` is not used by SLiM; it is free for you to use.

`type => (string$)`

The type of the script block; this will be `"early"` or `"late"` for the two types of Eidos events, or `"initialize"`, `"fitness"`, `"mateChoice"`, `"modifyChild"`, or `"recombination"` for the respective types of Eidos callbacks (see section 21.1 and chapter 22).

21.10.2 `SLiMEidosBlock` methods

`SLiMEidosBlock` provides no methods to modify a script block. You may, however, reschedule a block to run in a different set of generations using the `rescheduleScriptBlock()` method of `SLiMSim`, or register a new script block using the source and type of an existing block using the `register...()` methods of `SLiMSim` (see section 21.12.2).

21.11 Class SLiMgui

This class represents the SLiMgui application. When running under SLiMgui, a global `object` singleton constant of class `SLiMgui` will be defined, named `slimgui`. This object can be used to query and control the SLiMgui application. When running at the command line, the `slimgui` object will not exist; to determine whether the simulation is running under SLiMgui, one may therefore test `exists("slimgui")`. If a model needs to run both at the command line and under SLiMgui, all uses of the `slimgui` object should be protected by `if (exists("slimgui"))` to avoid errors.

21.11.1 `SLiMgui` properties

`pid => (integer$)`

The Un*x process identifier (commonly called the “pid”) of the running SLiMgui application. This can be useful for scripts that wish to use system calls to influence the SLiMgui application.

21.11.2 `SLiMgui` methods

`– (void)openDocument(string$ filePath)`

Open the document at `filePath` in SLiMgui, if possible. Supported document types include SLiM model files (typically with a `.slim` path extension), text files (typically with a `.txt` path extension, and opened as untitled model files), and PDF files (typically with a `.pdf` path extension). This can be particularly useful for opening PDF documents created by the simulation itself, often by sublaunching a plotting process in R or another environment; see section 13.11 for an example.

– (void)pauseExecution(string$ filePath)

Pauses a model that is playing in SLiMgui. This is essentially equivalent to clicking the "Play" button to stop the execution of the model. Execution can be resumed by the user, by clicking the "Play" button again; unlike calling `stop()` or `simulationFinished()`, the simulation is not terminated. This method can be useful for debugging or exploratory purposes, to pause the model at a point of interest. Execution is paused at the end of the currently executing generation, not mid-generation.

If the model is being profiled, or is executing forward to a generation number entered in the generation field, `pauseExecution()` will do nothing; by design, `pauseExecution()` only pauses execution when SLiMgui is doing a simple "Play" of the model.

21.12 Class SLiMSim

This class represents a SLiM simulation. The current `SLiMSim` instance is defined as a global constant named `sim`.

21.12.1 `SLiMSim` properties

chromosome => (object<Chromosome>$)

The `Chromosome object` used by the simulation.

chromosomeType => (string$)

The type of chromosome being simulated; this will be one of `"A"`, `"X"`, or `"Y"`.

dimensionality => (string$)

The spatial dimensionality of the simulation, as specified in `initializeSLiMOptions()`. This will be `""` (the empty string) for non-spatial simulations (the default), or `"x"`, `"xy"`, or `"xyz"`, for simulations using those spatial dimensions respectively.

dominanceCoeffX <–> (float$)

The dominance coefficient value used to modify the selection coefficients of mutations present on the single X chromosome of an XY male (see the SLiM documentation for details). Used only when simulating an X chromosome; setting a value for this property in other circumstances is an error. Changing this will normally affect the fitness values calculated at the end of the current generation; if you want current fitness values to be affected, you can call `SLiMSim`'s method `recalculateFitness()` – but see the documentation of that method for caveats.

generation <–> (integer$)

The current generation number.

genomicElementTypes => (object<GenomicElementType>)

The `GenomicElementType` objects being used in the simulation.

inSLiMgui => (logical$)

This property has been deprecated, and may be removed in a future release of SLiM. In SLiM 3.2.1 and later, use `exists("slimgui")` instead.

If `T`, the simulation is presently running inside SLiMgui; if `F`, it is running at the command line. In general simulations should not care where they are running, but in special circumstances such as opening plot windows it may be necessary to know the runtime environment.

interactionTypes => (object<InteractionType>)

The `InteractionType` objects being used in the simulation.

`modelType => (string$)`

The type of model being simulated, as specified in `initializeSLiMModelType()`. This will be `"WF"` for WF models (Wright-Fisher models, the default), or `"nonWF"` for nonWF models (non-Wright-Fisher models; see section 1.6 for discussion).

`mutationTypes => (object<MutationType>)`

The `MutationType` objects being used in the simulation.

`mutations => (object<Mutation>)`

The `Mutation` objects that are currently active in the simulation.

`periodicity => (string$)`

The spatial periodicity of the simulation, as specified in `initializeSLiMOptions()`. This will be `""` (the empty string) for non-spatial simulations and simulations with no periodic spatial dimensions (the default). Otherwise, it will be a string representing the subset of spatial dimensions that have been declared to be periodic, as specified to `initializeSLiMOptions()`.

`scriptBlocks => (object<SLiMEidosBlock>)`

All registered `SLiMEidosBlock` objects in the simulation.

`sexEnabled => (logical$)`

If `T`, sex is enabled in the simulation; if `F`, individuals are hermaphroditic.

`subpopulations => (object<Subpopulation>)`

The `Subpopulation` instances currently defined in the simulation.

`substitutions => (object<Substitution>)`

A vector of `Substitution` objects, representing all mutations that have been fixed.

`tag <–> (integer$)`

A user-defined `integer` value. The value of `tag` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code. The value of `tag` is not used by SLiM; it is free for you to use. See also the `getValue()` and `setValue()` methods, for another way of attaching state to the simulation.

21.12.2 `SLiMSim` methods

`– (object<Subpopulation>$)addSubpop(is$ subpopID, integer$ size, [float$ sexRatio = 0.5])`

Add a new subpopulation with id `subpopID` and `size` individuals. The `subpopID` parameter may be either an `integer` giving the ID of the new subpopulation, or a `string` giving the name of the new subpopulation (such as `"p5"` to specify an ID of 5). Only if sex is enabled in the simulation, the initial sex ratio may optionally be specified as `sexRatio` (as the male fraction, M:M+F); if it is not specified, a default of `0.5` is used. The new subpopulation will be defined as a global variable immediately by this method (see section 21.13), and will also be returned by this method. Subpopulations added by this method will initially consist of individuals with empty genomes. In order to model subpopulations that split from an already existing subpopulation, use `addSubpopSplit()`.

`– (object<Subpopulation>$)addSubpopSplit(is$ subpopID, integer$ size, io<Subpopulation>$ sourceSubpop, [float$ sexRatio = 0.5])`

Split off a new subpopulation with id `subpopID` and `size` individuals derived from subpopulation `sourceSubpop`. The `subpopID` parameter may be either an `integer` giving the ID of the new subpopulation, or a `string` giving the name of the new subpopulation (such as `"p5"` to specify an ID of 5). The `sourceSubpop` parameter may specify the source subpopulation either as a `Subpopulation` object or by `integer` identifier. Only if sex is enabled in the simulation, the initial sex ratio may optionally be specified as `sexRatio` (as the male fraction, M:M+F); if it is not specified, a default of `0.5` is used. The new subpopulation will be defined as a global variable immediately by this method (see section 21.13), and will also be returned by this method.

Subpopulations added by this method will consist of individuals that are clonal copies of individuals from the source subpopulation, randomly chosen with probabilities proportional to fitness. The fitness of all of these initial individuals is considered to be 1.0, to avoid a doubled round of selection in the initial generation, given that fitness values were already used to choose the individuals to clone. Once this initial set of individuals has mated to produce offspring, the model is effectively of parental individuals in the source subpopulation mating randomly according to fitness, as usual in SLiM, with juveniles migrating to the newly added subpopulation. Effectively, then, then new subpopulation is created empty, and is filled by migrating juveniles from the source subpopulation, in accordance with SLiM's usual model of juvenile migration.

– `(integer$)countOfMutationsOfType(io<MutationType>$ mutType)`

Returns the number of mutations that are of the type specified by `mutType`, out of all of the mutations that are currently active in the simulation. If you need a vector of the matching `Mutation` objects, rather than just a count, use `-mutationsOfType()`. This method is often used to determine whether an introduced mutation is still active (as opposed to being either lost or fixed). This method is provided for speed; it is much faster than the corresponding Eidos code.

– `(void)deregisterScriptBlock(io<SLiMEidosBlock> scriptBlocks)`

All `SLiMEidosBlock` objects specified by `scriptBlocks` (either with `SLiMEidosBlock` objects or with `integer` identifiers) will be scheduled for deregistration. The deregistered blocks remain valid, and may even still be executed in the current stage of the current generation (see section 22.8); the blocks are not actually deregistered and deallocated until sometime after the currently executing script block has completed. To immediately prevent a script block from executing, even when it is scheduled to execute in the current stage of the current generation, use the `active` property of the script block (see sections 20.10.1 and 21.8).

– `(+)getValue(string$ key)`

Returns the value previously set for the dictionary entry identifier `key` using `setValue()`, or `NULL` if no value has been set. This dictionary-style functionality is actually provided by the superclass of `SLiMSim`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

– `(integer)mutationCounts(No<Subpopulation> subpops,`
  `[No<Mutation> mutations = NULL])`

Return an `integer` vector with the frequency counts of all of the `Mutation` objects passed in `mutations`, within the `Subpopulation` objects in `subpops`. The `subpops` argument is required, but you may pass `NULL` to get population-wide frequency counts. If the optional `mutations` argument is `NULL` (the default), frequency counts will be returned for all of the active `Mutation` objects in the simulation – the same `Mutation` objects, and in the same order, as would be returned by the `mutations` property of `sim`, in other words.

See the `-mutationFrequencies()` method to obtain `float` frequencies instead of `integer` counts.

– `(float)mutationFrequencies(No<Subpopulation> subpops,`
  `[No<Mutation> mutations = NULL])`

Return a `float` vector with the frequencies of all of the `Mutation` objects passed in `mutations`, within the `Subpopulation` objects in `subpops`. The `subpops` argument is required, but you may pass `NULL` to get population-wide frequencies. If the optional `mutations` argument is `NULL` (the default), frequencies will be returned for all of the active `Mutation` objects in the simulation – the same `Mutation` objects, and in the same order, as would be returned by the `mutations` property of `sim`, in other words.

See the `-mutationCounts()` method to obtain `integer` counts instead of `float` frequencies.

– `(object<Mutation>)mutationsOfType(io<MutationType>$ mutType)`

Returns an `object` vector of all the mutations that are of the type specified by `mutType`, out of all of the mutations that are currently active in the simulation. If you just need a count of the matching `Mutation` objects, rather than a vector of the matches, use `–countOfMutationsOfType()`. This method is often used to look up an introduced mutation at a later point in the simulation, since there is no way to keep persistent references to objects in SLiM. This method is provided for speed; it is much faster than the corresponding Eidos code.

– `(void)outputFixedMutations([Ns$ filePath = NULL], [logical$ append = F])`

Output all fixed mutations – all `Substitution` objects, in other words (see section 4.2.4) – in a SLiM native format (see section 23.1.2 for output format details). If the optional parameter `filePath` is `NULL` (the default), output will be sent to Eidos's output stream (see section 4.2.1). Otherwise, output will be sent to the filesystem path specified by `filePath`, overwriting that file if `append` if `F`, or appending to the end of it if `append` is `T`. Mutations which have fixed but have not been turned into `Substitution` objects – typically because `convertToSubstitution` has been set to `F` for their mutation type (see section 21.9.1) – are not output; they are still considered to be segregating mutations by SLiM.

Output is generally done in a `late()` event, so that the output reflects the state of the simulation at the end of a generation.

– `(void)outputFull([Ns$ filePath = NULL], [logical$ binary = F],`
  `[logical$ append = F], [logical$ spatialPositions = T], [logical$ ages = T])`

Output the state of the entire population (see section 23.1.1 for output format details). If the optional parameter `filePath` is `NULL` (the default), output will be sent to Eidos's output stream (see section 4.2.1). Otherwise, output will be sent to the filesystem path specified by `filePath`, overwriting that file if `append` if `F`, or appending to the end of it if `append` is `T`. When writing to a file, a `logical` flag, `binary`, may be supplied as well. If `binary` is `T`, the population state will be written as a binary file instead of a text file (binary data cannot be written to the standard output stream). The binary file is usually smaller, and in any case will be read much faster than the corresponding text file would be read. Binary files are not guaranteed to be portable between platforms; in other words, a binary file written on one machine may not be readable on a different machine (but in practice it usually will be, unless the platforms being used are fairly unusual). If `binary` is `F` (the default), a text file will be written.

Beginning with SLiM 2.3, the `spatialPositions` parameter may be used to control the output of the spatial positions of individuals in simulations for which continuous space has been enabled using the `dimensionality` option of `initializeSLiMOptions()`. If `spatialPositions` is `F`, the output will not contain spatial positions, and will be identical to the output generated by SLiM 2.1 and later. If `spatialPositions` is `T`, spatial position information will be output if it is available (see section 23.1.1 for format details). If the simulation does not have continuous space enabled, the `spatialPositions` parameter will be ignored. Positional information may be output for all output destinations – the Eidos output stream, a text file, or a binary file.

Beginning with SLiM 3.0, the `ages` parameter may be used to control the output of the ages of individuals in nonWF simulations. If `ages` is `F`, the output will not contain ages, preserving backward compatibility with the output format of SLiM 2.1 and later. If `ages` is `T`, ages will be output for nonWF models (see section 23.1.1 for format details). In WF simulations, the ages parameter will be ignored.

Output is generally done in a `late()` event, so that the output reflects the state of the simulation at the end of a generation.

– `(void)outputMutations(object<Mutation> mutations, [Ns$ filePath = NULL],`
  `[logical$ append = F])`

Output all of the given mutations (see section 23.1.3 for output format details). This can be used to output all mutations of a given mutation type, for example. If the optional parameter `filePath` is `NULL` (the default), output will be sent to Eidos's output stream (see section 4.2.1). Otherwise, output will be sent to the filesystem path specified by `filePath`, overwriting that file if `append` if `F`, or appending to the end of it if `append` is `T`.

Output is generally done in a `late()` event, so that the output reflects the state of the simulation at the end of a generation.

– `(void)outputUsage(void)`

Output the current memory usage of the simulation to Eidos's output stream. The specifics of what is printed, and in what format, should not be relied upon as they may change from version to version of SLiM. This method is primarily useful for understanding where the memory usage of a simulation predominantly resides, for debugging or optimization. Note that it does not capture *all* memory usage by the process; rather, it summarizes the memory usage by SLiM and Eidos in directly allocated objects and buffers. To get the *total* memory usage of the running process (either current or peak), use the Eidos function `usage()`.

– `(integer$)readFromPopulationFile(string$ filePath)`

Read from a population initialization file, whether in text or binary format as previously specified to `outputFull()`, and return the generation counter value represented by the file's contents (i.e., the generation at which the file was generated). Although this is most commonly used to set up initial populations (often in an Eidos event set to run in generation 1, immediately after simulation initialization), it may be called in any Eidos event; the current state of all populations will be wiped and replaced by the state in the file at `filePath`. All Eidos variables that are of type `object` and have element type `Subpopulation`, `Genome`, `Mutation`, `Individual`, or `Substitution` will be removed as a side effect of this method, since all such variables would refer to objects that no longer exist in the SLiM simulation; if you want to preserve any of that state, you should output it or save it to a file prior to this call. New symbols will be defined to refer to the new `Subpopulation` objects loaded from the file.

If the file being read was written by a version of SLiM prior to 2.3, then for backward compatibility fitness values will be calculated immediately for any new subpopulations created by this call, which will trigger the calling of any activated and applicable `fitness()` callbacks. When reading files written by SLiM 2.3 or later, fitness values are not calculated as a side effect of this call (because the simulation will often need to evaluate interactions or modify other state prior to doing so).

In SLiM 2.3 and later when using the WF model, calling `readFromPopulationFile()` from any context other than a `late()` event causes a warning; calling from a `late()` event is almost always correct in WF models, so that fitness values can be automatically recalculated by SLiM at the usual time in the generation cycle without the need to force their recalculation (see chapter 19, and comments on `recalculateFitness()` below).

In SLiM 3.0 when using the nonWF model, calling `readFromPopulationFile()` from any context other than an `early()` event causes a warning; calling from an `early()` event is almost always correct in nonWF models, so that fitness values can be automatically recalculated by SLiM at the usual time in the generation cycle without the need to force their recalculation (see chapter 20, and comments on `recalculateFitness()` below).

As of SLiM 2.1, this method changes the generation counter to the generation read from the file. If you do not want the generation counter to be changed, you can change it back after reading, by setting `sim.generation` to whatever value you wish. Note that restoring a saved past state and running forward again will not yield the same simulation results, because the random number generator's state will not be the same; to ensure reproducibility from a given time point, `setSeed()` can be used to establish a new seed value. Any changes made to the simulation's structure (mutation types, genomic element types, etc.) will not be wiped and re-established by `readFromPopulationFile()`; this method loads only the population's state, not the simulation configuration, so care should be taken to ensure that the simulation structure meshes coherently with the loaded data. Indeed, state such as the selfing and cloning rates of subpopulations, values set into `tag` properties, and values set onto objects with `setValue()` will also be lost, since it is not saved out by outputFull(). Only information saved by `outputFull()` will be restored; all other state associated with the simulation's subpopulations, individuals, genomes, mutations, and substitutions will be lost, and should be re-established by the model if it is still needed.

As of SLiM 2.3, this method will read and restore the spatial positions of individuals if that information is present in the output file and the simulation has enabled continuous space (see `outputFull()` for details). If spatial positions are present in the output file but the simulation has not enabled continuous space (or the number of spatial dimensions does not match), an error will result. If the simulation has enabled continuous space but spatial positions are not present in the output file, the spatial positions of the individuals read will be undefined, but an error is not raised.

As of SLiM 3.0, this method will read and restore the ages of individuals if that information is present in the output file and the simulation is based upon the nonWF model. If ages are present but the simulation uses a WF model, an error will result; the WF model does not use age information. If ages are not present but the simulation uses a nonWF model, an error will also result; the nonWF model requires age information.

– `(void)recalculateFitness([Ni$ generation = NULL])`

Force an immediate recalculation of fitness values for all individuals in all subpopulations. Normally fitness values are calculated at a fixed point in each generation, and those values are cached and used throughout the following generation. If simulation parameters are changed in script in a way that affects fitness calculations, and if you wish those changes to take effect immediately rather than taking effect at the end of the current generation, you may call `recalculateFitness()` to force an immediate recalculation and recache.

The optional parameter `generation` provides the generation for which `fitness()` callbacks should be selected; if it is `NULL` (the default), the simulation's current generation value, `sim.generation`, is used. If you call `recalculateFitness()` in an `early()` event in a WF model, you may wish this to be `sim.generation - 1` in order to utilize the `fitness()` callbacks for the previous generation, as if the changes that you have made to fitness-influencing parameters were already in effect at the end of the previous generation when the new generation was first created and evaluated (usually it is simpler to just make such changes in a `late()` event instead, however, in which case calling `recalculateFitness()` is probably not necessary at all since fitness values will be recalculated immediately afterwards). Regardless of the value supplied for `generation` here, `sim.generation` inside `fitness()` callbacks will report the true generation number, so if your callbacks consult that parameter in order to create generation-specific fitness effects you will need to handle the discrepancy somehow. (Similar considerations apply for nonWF models that call `recalculateFitness()` in a `late()` event, which is also not advisable in general.)

After this call, the fitness values used for all purposes in SLiM will be the newly calculated values. Calling this method will trigger the calling of any enabled and applicable `fitness()` callbacks, so this is quite a heavyweight operation; you should think carefully about what side effects might result (which is why fitness recalculation does not just occur automatically after changes that might affect fitness values).

– `(object<SLiMEidosBlock>$)registerEarlyEvent(Nis$ id, string$ source,`
  `[Ni$ start = NULL], [Ni$ end = NULL])`

Register a block of Eidos source code, represented as the `string` singleton `source`, as an Eidos `early()` event in the current simulation, with optional `start` and `end` generations limiting its applicability. The script block will be given identifier `id` (specified as an `integer`, or as a `string` symbolic name such as `"s5"`); this may be `NULL` if there is no need to be able to refer to the block later. The registered event is added to the end of the list of registered `SLiMEidosBlock` objects, and is active immediately; it *may* be eligible to execute in the current generation (see section 22.8 for details). The new `SLiMEidosBlock` will be defined as a global variable immediately by this method (see section 21.10), and will also be returned by this method.

– `(object<SLiMEidosBlock>$)registerFitnessCallback(Nis$ id, string$ source, Nio<MutationType>$ mutType, [Nio<Subpopulation>$ subpop = NULL], [Ni$ start = NULL], [Ni$ end = NULL])`

Register a block of Eidos source code, represented as the `string` singleton `source`, as an Eidos `fitness()` callback in the current simulation, with a required mutation type `mutType` (which may be an `integer` mutation type identifier, or `NULL` to indicate a global `fitness()` callback – see section 22.2), optional subpopulation `subpop` (which may also be an `integer` identifier, or `NULL`, the default, to indicate all subpopulations), and optional `start` and `end` generations all limiting its applicability. The script block will be given identifier `id` (specified as an `integer`, or as a `string` symbolic name such as `"s5"`); this may be `NULL` if there is no need to be able to refer to the block later. The registered callback is added to the end of the list of registered `SLiMEidosBlock` objects, and is active immediately; it *may* be eligible to execute in the current generation (see section 22.8 for details). The new `SLiMEidosBlock` will be defined as a global variable immediately by this method (see section 21.10), and will also be returned by this method.

– `(object<SLiMEidosBlock>$)registerInteractionCallback(Nis$ id, string$ source, io<InteractionType>$ intType, [Nio<Subpopulation>$ subpop = NULL], [Ni$ start = NULL], [Ni$ end = NULL])`

Register a block of Eidos source code, represented as the `string` singleton `source`, as an Eidos `interaction()` callback in the current simulation, with a required interaction type `intType` (which may be an `integer` identifier), optional subpopulation `subpop` (which may also be an `integer` identifier, or `NULL`, the default, to indicate all subpopulations), and optional `start` and `end` generations all limiting its applicability. The script block will be given identifier `id` (specified as an `integer`, or as a `string` symbolic name such as `"s5"`); this may be `NULL` if there is no need to be able to refer to the block later. The registered callback is added to the end of the list of registered `SLiMEidosBlock` objects, and is active immediately; it will be eligible to execute the next time an `InteractionType` is evaluated. The new `SLiMEidosBlock` will be defined as a global variable immediately by this method (see section 21.10), and will also be returned by this method.

– `(object<SLiMEidosBlock>$)registerLateEvent(Nis$ id, string$ source, [Ni$ start = NULL], [Ni$ end = NULL])`

Register a block of Eidos source code, represented as the `string` singleton `source`, as an Eidos `late()` event in the current simulation, with optional `start` and `end` generations limiting its applicability. The script block will be given identifier `id` (specified as an `integer`, or as a `string` symbolic name such as `"s5"`); this may be `NULL` if there is no need to be able to refer to the block later. The registered event is added to the end of the list of registered `SLiMEidosBlock` objects, and is active immediately; it *may* be eligible to execute in the current generation (see section 22.8 for details). The new `SLiMEidosBlock` will be defined as a global variable immediately by this method (see section 21.10), and will also be returned by this method.

– `(object<SLiMEidosBlock>$)registerMateChoiceCallback(Nis$ id, string$ source, [Nio<Subpopulation>$ subpop = NULL], [Ni$ start = NULL], [Ni$ end = NULL])`

Register a block of Eidos source code, represented as the `string` singleton `source`, as an Eidos `mateChoice()` callback in the current simulation, with optional subpopulation `subpop` (which may be an `integer` identifier, or `NULL`, the default, to indicate all subpopulations) and optional `start` and `end` generations all limiting its applicability. The script block will be given identifier `id` (specified as an `integer`, or as a `string` symbolic name such as `"s5"`); this may be `NULL` if there is no need to be able to refer to the block later. The registered callback is added to the end of the list of registered `SLiMEidosBlock` objects, and is active immediately; it *may* be eligible to execute in the current generation (see section 22.8 for details). The new `SLiMEidosBlock` will be defined as a global variable immediately by this method (see section 21.10), and will also be returned by this method.

– `(object<SLiMEidosBlock>$)registerModifyChildCallback(Nis$ id, string$ source, [Nio<Subpopulation>$ subpop = NULL], [Ni$ start = NULL], [Ni$ end = NULL])`

Register a block of Eidos source code, represented as the `string` singleton `source`, as an Eidos `modifyChild()` callback in the current simulation, with optional subpopulation `subpop` (which may be an `integer` identifier, or `NULL`, the default, to indicate all subpopulations) and optional `start` and `end` generations all limiting its applicability. The script block will be given identifier `id` (specified as an `integer`, or as a `string` symbolic name such as `"s5"`); this may be `NULL` if there is no need to be able to refer to the block later. The registered callback is added to the end of the list of registered `SLiMEidosBlock` objects, and is active immediately; it *may* be eligible to execute in the current generation (see section 22.8 for details). The new `SLiMEidosBlock` will be defined as a global variable immediately by this method (see section 21.10), and will also be returned by this method.

– `(object<SLiMEidosBlock>$)registerRecombinationCallback(Nis$ id, string$ source, [Nio<Subpopulation>$ subpop = NULL], [Ni$ start = NULL], [Ni$ end = NULL])`

Register a block of Eidos source code, represented as the `string` singleton `source`, as an Eidos `recombination()` callback in the current simulation, with optional subpopulation `subpop` (which may be an `integer` identifier, or `NULL`, the default, to indicate all subpopulations) and optional `start` and `end` generations all limiting its applicability. The script block will be given identifier `id` (specified as an `integer`, or as a `string` symbolic name such as `"s5"`); this may be `NULL` if there is no need to be able to refer to the block later. The registered callback is added to the end of the list of registered `SLiMEidosBlock` objects, and is active immediately; it *may* be eligible to execute in the current generation (see section 22.8 for details). The new `SLiMEidosBlock` will be defined as a global variable immediately by this method (see section 21.10), and will also be returned by this method.

– `(object<SLiMEidosBlock>$)registerReproductionCallback(Nis$ id, string$ source, [Nio<Subpopulation>$ subpop = NULL], [Ns$ sex = NULL], [Ni$ start = NULL], [Ni$ end = NULL])`

Register a block of Eidos source code, represented as the `string` singleton `source`, as an Eidos `reproduction()` callback in the current simulation, with optional subpopulation `subpop` (which may be an `integer` identifier, or `NULL`, the default, to indicate all subpopulations), optional sex-specificity `sex` (which may be `"M"` or `"F"` in sexual simulations to make the callback specific to males or females respectively, or `NULL` for no sex-specificity), and optional `start` and `end` generations all limiting its applicability. The script block will be given identifier `id` (specified as an `integer`, or as a `string` symbolic name such as `"s5"`); this may be `NULL` if there is no need to be able to refer to the block later. The registered callback is added to the end of the list of registered `SLiMEidosBlock` objects, and is active immediately; it *may* be eligible to execute in the current generation (see section 22.8 for details). The new `SLiMEidosBlock` will be defined as a global variable immediately by this method (see section 21.10), and will also be returned by this method.

– `(object<SLiMEidosBlock>)rescheduleScriptBlock(object<SLiMEidosBlock>$ block, integer$ start, [Ni$ end = NULL], [Ni generations = NULL])`

Reschedule the target script block given by `block` to execute in a specified set of generations.

The first way to specify the generation set is with `start` and `end` parameter values; `block` will then execute from `start` to `end`, inclusive. In this case, `block` is returned.

The second way to specify the generation set is using the `generations` parameter; this is more flexible but more complicated. Since script blocks execute across a contiguous span of generations defined by their `start` and `end` properties, this may result in the duplication of `block`; one script block will be used for each contiguous span of generations in `generations`. The `block` object itself will be rescheduled to cover the first such span, whereas duplicates of `block` will be created to cover subsequent contiguous spans. A vector containing all of the script blocks scheduled by this method, including `block`, will be returned; this vector is guaranteed to be sorted by the (ascending) scheduled execution order of the blocks. Any duplicates of `block` created will be given values for the `active`, `source`, `tag`, and `type` properties equal to the current values for `block`, but will be given an `id` of `–1` since script block identifiers must be unique; if it is necessary to find the duplicated blocks again later, their `tag` property should be used. The vector supplied for `generations` does not need to be in sorted order, but it must not contain any duplicates.

Because this method can create a large number of duplicate script blocks, it can sometimes be better to handle script block scheduling in other ways. If an `early()` event needs to execute every tenth generation over the whole duration of a long model run, for example, it would not be advisable to use a call like `sim.rescheduleScriptBlock(s1, generations=seq(10, 100000, 10))` for that purpose, since that would result in thousands of duplicate script blocks. Instead, it would be preferable to add a test such as `if (sim.generation % 10 != 0) return;` at the beginning of the event. It is legal to reschedule a script block while the block is executing; a call like `sim.rescheduleScriptBlock(self, sim.generation + 10, sim.generation + 10);` made inside a given block would therefore also cause the block to execute every tenth generation, although this sort of self-rescheduling code is probably harder to read, maintain, and debug.

Whichever way of specifying the generation set is used, the discussion in section 22.8 applies: `block` may continue to be executed during the current life cycle stage even after it has been rescheduled, unless it is made inactive using its `active` property, and similarly, the block may not execute during the current life cycle stage if it was not already scheduled to do so. Rescheduling script blocks during the generation and life cycle stage in which they are executing, or in which they are intended to execute, should be avoided.

Note that new script blocks can also be created and scheduled using the `register...()` methods of `SLiMSim`; by using the same source as a template script block, the template can be duplicated and scheduled for different generations. In fact, `rescheduleScriptBlock()` does essentially that internally.

– `(void)setValue(string$ key, + value)`

Sets a value for the dictionary entry identifier `key`. The value, which may be of any type other than `object`, can be fetched later using `getValue()`. This dictionary-style functionality is actually provided by the superclass of `SLiMSim`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

– `(void)simulationFinished(void)`

Declare the current simulation finished. Normally SLiM ends a simulation when, at the end of a generation, there are no script events or callbacks registered for any future generation (excluding scripts with no declared end generation). If you wish to end a simulation before this condition is met, a call to `simulationFinished()` will cause the current simulation to end at the end of the current generation. For example, a simulation might self-terminate if a test for a dynamic equilibrium condition is satisfied. Note that the current generation will finish executing; if you want the simulation to stop immediately, you can use the Eidos method `stop()`, which raises an error condition.

– `(logical$)treeSeqCoalesced(void)`

Returns the coalescence state for the recorded tree sequence at the last simplification. The returned value is a logical singleton flag, `T` to indicate that full coalescence was observed at the last tree-sequence simplification (meaning that there is a single ancestral individual that roots all ancestry trees at all sites along the chromosome – although not necessarily the *same* ancestor at all sites), or `F` if full coalescence was not observed. For simple models, reaching coalescence may indicate that the model has reached an equilibrium state, but this may not be true in models that modify the dynamics of the model during execution by changing migration rates, introducing new mutations programmatically, dictating non-random mating, etc., so be careful not to attach more meaning to coalescence than it is due; some models may require burn-in beyond coalescence to reach equilibrium, or may not have an equilibrium state at all. Also note that some actions by a model, such as adding a new subpopulation, may cause the coalescence state to revert from `T` back to `F` (at the next simplification), so a return value of `T` may not necessarily mean that the model is coalesced at the present moment – only that it *was* coalesced at the last simplification.

This method may only be called if tree sequence recording has been turned on with `initializeTreeSeq()`; in addition, `checkCoalescence=T` must have been supplied to `initializeTreeSeq()`, so that the necessary work is done during each tree-sequence simplification. Since this method does not perform coalescence checking itself, but instead simply returns the coalescence state observed at the last simplification, it may be desirable to call `treeSeqSimplify()` immediately before `treeSeqCoalesced()` to obtain up-to-date information. However, the speed penalty of doing this in every generation would be large, and most models do not need this level of precision; usually it is sufficient to know that the model has coalesced, without knowing whether that happened in the current generation or in a recent preceding generation.

– `(void)treeSeqOutput(string$ path, [logical$ simplify = T])`

Outputs the current tree sequence recording tables to the path specified by path. This method may only be called if tree sequence recording has been turned on with `initializeTreeSeq()`. If `simplify` is `T` (the default), simplification will be done immediately prior to output; this is almost always desirable, unless a model wishes to avoid simplification entirely. A binary tree sequence file will be written to the specified path; a filename extension of `.trees` is suggested for this type of file.

– `(void)treeSeqRememberIndividuals(object<Individual> individuals)`

Permanently adds the individuals specified by `individuals` to the sample retained across tree sequence table simplification. This method may only be called if tree sequence recording has been turned on with `initializeTreeSeq()`. All currently living individuals are always retained across simplification; this method does not need to be called, and indeed should not be called, for that purpose. Instead, `treeSeqRememberIndividuals()` is for *permanently* adding particular individuals to the retained sample. Typically this would be used, for example, to retain particular individuals that you wanted to be able to trace ancestry back to in later analysis. However, this is not the typical usage pattern for tree sequence recording; most models will not need to call this method.

The metadata (age, location, etc) that are stored in the resulting tree sequence are those values present at either (a) the final generation, if the individual is alive at the end of the simulation, or (b) the last time that the individual was remembered, if not. Calling `treeSeqRememberIndividuals()` on an individual that is already remembered will cause the archived information about the remembered individual to be updated to reflect the individual's current state. A case where this is particularly important is for the spatial location of individuals in continuous-space models. SLiM automatically remembers the individuals that comprise the first generation of any new subpopulation created with `addSubpop()`, for easy recapitation and other analysis (see section 16.10). However, since these first-generation individuals are remembered at the moment they are created, their spatial locations have not yet been set up, and will contain garbage – and those garbage values will be archived in their remembered state. If you need correct spatial locations of first-generation individuals for your post-simulation analysis, you should call `treeSeqRememberIndividuals()` explicitly on the first generation, after setting spatial locations, to update the archived information with the correct spatial positions.

– `(void)treeSeqSimplify(void)`

Triggers an immediate simplification of the tree sequence recording tables. This method may only be called if tree sequence recording has been turned on with `initializeTreeSeq()`. A call to this method will free up memory being used by entries that are no longer in the ancestral path of any individual within the current sample (currently living individuals, in other words, plus those explicitly added to the sample with `treeSeqRememberIndividuals()`), but it can also take a significant amount of time. Typically calling this method is not necessary; the automatic simplification performed occasionally by SLiM should be sufficient for most models.

21.13 Class Subpopulation

This class represents one subpopulation in the simulated population. Section 1.5.5 presents an overview of the conceptual role of this class. The subpopulations currently defined in the simulation are defined as global constants with the same names used in the SLiM input file – `p1`, `p2`, and so forth.

21.13.1 `Subpopulation` *properties*

`cloningRate => (float)`

The fraction of children in the next generation that will be produced by cloning (as opposed to biparental mating). In non-sexual (i.e. hermaphroditic) simulations, this property is a singleton `float` representing the overall subpopulation cloning rate. In sexual simulations, this property is a `float` vector with two values: the cloning rate for females (at index `0`) and for males (at index `1`).

`firstMaleIndex => (integer$)`

The index of the first male individual in the subpopulation. The `genomes` vector is sorted into females first and males second; `firstMaleIndex` gives the position of the boundary between those sections. Note, however, that there are two genomes per diploid individual, and the `firstMaleIndex` is *not* premultiplied by `2`; you must multiply it by `2` before using it to decide whether a given index into `genomes` is a genome for a male or a female. The `firstMaleIndex` property is also the number of females in the subpopulation, given this design. For non-sexual (i.e. hermaphroditic) simulations, this property has an undefined value and should not be used.

`fitnessScaling <–> (float$)`

A `float` scaling factor applied to the fitness of all individuals in this subpopulation (i.e., the fitness value computed for each individual will be multiplied by this value). This is primarily of use in nonWF models, where fitness is absolute, rather than in WF models, where fitness is relative (and thus a constant factor multiplied into the fitness of every individual will make no difference); however, it may be used in either type of model. This provides a simple, fast way to modify the fitness of all individuals in a subpopulation; conceptually it is similar to returning the same fitness effect for all individuals in the subpopulation from a `fitness(NULL)` callback, but without the complexity and performance overhead of implementing such a callback. To scale the fitness of individuals by different (individual-specific) factors, see the `fitnessScaling` property of `Individual`.

The value of `fitnessScaling` is reset to `1.0` every generation, so that any scaling factor set lasts for only a single generation. This reset occurs immediately after fitness values are calculated, in both WF and nonWF models.

`genomes => (object<Genome>)`

All of the genomes contained by the subpopulation; there are two genomes per diploid individual.

`id => (integer$)`

The identifier for this subpopulation; for subpopulation `p3`, for example, this is `3`.

`immigrantSubpopFractions => (float)`

The expected value of the fraction of children in the next generation that are immigrants arriving from particular subpopulations.

`immigrantSubpopIDs => (integer)`

The identifiers of the particular subpopulations from which immigrants will arrive in the next generation.

`individualCount => (integer$)`

The number of individuals in the subpopulation; one-half of the number of genomes.

`individuals => (object<Individual>)`

All of the individuals contained by the subpopulation. Each individual is diploid and thus contains two `Genome` objects. See the `sampleIndividuals()` and `subsetIndividuals()` for fast ways to get a subset of the individuals in a subpopulation.

`selfingRate => (float$)`

The expected value of the fraction of children in the next generation that will be produced by selfing (as opposed to biparental mating). Selfing is only possible in non-sexual (i.e. hermaphroditic) simulations; for sexual simulations this property always has a value of `0.0`.

`sexRatio => (float$)`

For sexual simulations, the sex ratio for the subpopulation. This is defined, in SLiM, as the fraction of the subpopulation that is male; in other words, it is actually the M:(M+F) ratio. For non-sexual (i.e. hermaphroditic) simulations, this property has an undefined value and should not be used.

`spatialBounds => (float)`

The spatial boundaries of the subpopulation. The length of the `spatialBounds` property depends upon the spatial dimensionality declared with `initializeSLiMOptions()`. If the spatial dimensionality is zero (as it is by default), the value of this property is `float(0)` (a zero-length `float` vector). Otherwise, minimums are supplied for each coordinate used by the dimensionality of the simulation, followed by maximums for each. In other words, if the declared dimensionality is `"xy"`, the `spatialBounds` property will contain values `(x0, y0, x1, y1)`; bounds for the *z* coordinate will not be included in that case, since that coordinate is not used in the simulation's dimensionality. This property cannot be set, but the `setSpatialBounds()` method may be used to achieve the same thing.

`tag <–> (integer$)`

A user-defined `integer` value. The value of `tag` is initially undefined (i.e., has an effectively random value that could be different every time you run your model); if you wish it to have a defined value, you must arrange that yourself by explicitly setting its value prior to using it elsewhere in your code. The value of `tag` is not used by SLiM; it is free for you to use. See also the `getValue()` and `setValue()` methods, for another way of attaching state to subpopulations.

21.13.2 `Subpopulation` methods

`– (No<Individual>$)addCloned(object<Individual>$ parent)`

Generates a new offspring individual from the given parent by clonal reproduction, queues it for addition to the target subpopulation, and returns it. The new offspring will not be visible as a member of the target subpopulation until the end of the offspring generation life cycle stage. The subpopulation of `parent` will be used to locate applicable `modifyChild()` callbacks governing the generation of the offspring individual.

Note that this method is only for use in nonWF models. See `addCrossed()` for further general notes on the addition of new offspring individuals.

```
– (No<Individual>$)addCrossed(object<Individual>$ parent1,
    object<Individual>$ parent2, [Nfs$ sex = NULL])
```

Generates a new offspring individual from the given parents by biparental sexual reproduction, queues it for addition to the target subpopulation, and returns it. The new offspring will not be visible as a member of the target subpopulation until the end of the offspring generation life cycle stage. Attempting to use a newly generated offspring individual as a mate, or to reference it as a member of the target subpopulation in any other way, will result in an error. In most models the returned individual is not used, but it is provided for maximal generality and flexibility.

The new offspring individual is generated from `parent1` and `parent2` by crossing them. In sexual models `parent1` must be female and `parent2` must be male; in hermaphroditic models, `parent1` and `parent2` are unrestricted. If `parent1` and `parent2` are the same individual in a hermaphroditic model, that parent self-fertilizes, or “selfs”, to generate the offspring sexually (note this is not the same as clonal reproduction). Such selfing is considered “incidental” by `addCrossed()`, however; if the `preventIncidentalSelfing` flag of `initializeSLiMOptions()` is `T`, supplying the same individual for `parent1` and `parent2` is an error (you must check for and prevent incidental selfing if you set that flag in a nonWF model). If non-incidental selfing is desired, `addSelfed()` should be used instead.

The `sex` parameter specifies the sex of the offspring. A value of `NULL` means "make the default choice"; in non-sexual models it is the only legal value for `sex`, and does nothing, whereas in sexual models it causes male or female to be chosen with equal probability. A value of `"M"` or `"F"` for `sex` specifies that the offspring should be male or female, respectively. Finally, a `float` value from `0.0` to `1.0` for `sex` provides the probability that the offspring will be male; a value of `0.0` will produce a female, a value of `1.0` will produce a male, and for intermediate values SLiM will draw the sex of the offspring randomly according to the specified probability. Unless you wish the bias the sex ratio of offspring, the default value of `NULL` should generally be used.

Note that any defined, active, and applicable `recombination()` and `modifyChild()` callbacks will be called as a side effect of calling this method, before this method even returns. For `recombination()` callbacks, the subpopulation of the parent that is generating a given gamete is used; for `modifyChild()` callbacks the situation is more complex. In most biparental mating events, `parent1` and `parent2` will belong to the same subpopulation, and `modifyChild()` callbacks for that subpopulation will be used, just as in WF models. In certain models (such as models of pollen flow and broadcast spawning), however, biparental mating may occur between parents that are not from the same subpopulation; that is legal in nonWF models, and in that case, `modifyChild()` callbacks for the subpopulation of `parent1` are used (since that is the maternal parent).

If the `modifyChild()` callback process results in rejection of the proposed child (see section 22.4), a new offspring individual will not be generated, and this method will return `NULL`. To force the generation of an offspring individual from a given pair of parents, you could loop until `addCrossed()` succeeds, but note that if your `modifyChild()` callback rejects all proposed children from those particular parents, your model will then hang, so care must be taken with this approach. Usually, nonWF models do not force generation of offspring in this manner; rejection of a proposed offspring by a `modifyChild()` callback typically represents a phenomenon such as post-mating reproductive isolation or lethal genetic incompatibilities that would reduce the expected litter size, so the default behavior is typically desirable.

Note that this method is only for use in nonWF models, in which offspring generation is managed manually by the model script; in such models, `addCrossed()` must be called only from `reproduction()` callbacks, and may not be called at any other time. In WF models, offspring generation is managed automatically by the SLiM core.

```
– (No<Individual>$)addEmpty([Nfs$ sex = NULL])
```

Generates a new offspring individual with empty genomes (i.e., containing no mutations), queues it for addition to the target subpopulation, and returns it. The new offspring will not be visible as a member of the target subpopulation until the end of the offspring generation life cycle stage. No `recombination()` callbacks will be called. The target subpopulation will be used to locate applicable `modifyChild()` callbacks governing the generation of the offspring individual (unlike the other `addX()` methods, because there is no parental individual to reference). The offspring is considered to have no parents for the purposes of pedigree tracking. The `sex` parameter is treated as in `addCrossed()`.

Note that this method is only for use in nonWF models. See `addCrossed()` for further general notes on the addition of new offspring individuals.

```
– (No<Individual>$)addRecombinant(No<Genome>$ strand1, No<Genome>$ strand2,
    Ni breaks1, No<Genome>$ strand3, No<Genome>$ strand4, Ni breaks2,
    [Nfs$ sex = NULL])
```

Generates a new offspring individual from the given parental genomes with the specified recombination breakpoints, queues it for addition to the target subpopulation, and returns it. The new offspring will not be visible as a member of the target subpopulation until the end of the offspring generation life cycle stage. The target subpopulation will be used to locate applicable `modifyChild()` callbacks governing the generation of the offspring individual (unlike the other addX() methods, because there is no parental individual to reference); recombination() callbacks will not be called by this method. This method is an advanced feature; most models will use addCrossed(), addSelfed(), or addCloned() instead.

This method supports several possible configurations for strand1, strand2, and breaks1 (and the same applies for strand3, strand4, and breaks2). If strand1 and strand2 are both NULL, the corresponding genome in the generated offspring will be empty, as from addEmpty(), with no parental genomes and no added mutations; in this case, breaks1 must be NULL or zero-length. If strand1 is non-NULL but strand2 is NULL, the corresponding genome in the generated offspring will be a clonal copy of strand1 with mutations added, as from addCloned(); in this case, breaks1 must similarly be NULL or zero-length. If strand1 and strand2 are both non-NULL, the corresponding genome in the generated offspring will result from recombination between strand1 and strand2 with mutations added, as from addCrossed(), with strand1 being the initial copy strand; copying will switch between strands at each breakpoint in breaks1, which must be non-NULL but need not be sorted or uniqued (SLiM will sort and unique the supplied breakpoints internally). (It is not currently legal for strand1 to be NULL and strand2 non-NULL; that variant may be assigned some meaning in future.) Again, this discussion applies equally to strand3, strand4, and breaks2, *mutatis mutandis*. Note that when new mutations are generated by addRecombinant(), their subpopID property will be the id of the offspring's subpopulation, since the parental subpopulation is ambiguous in the general case; this behavior differs from the other add...() methods.

The sex parameter is interpreted exactly as in addCrossed(); see that method for discussion. If the offspring sex is specified in any way (i.e., if sex is non-NULL), the strands provided must be compatible with the sex chosen. If the offspring sex is not specified (i.e., if sex is NULL), the sex will be inferred from the strands provided where possible (when modeling an X or Y chromosome), or will be chosen randomly otherwise (when modeling autosomes); it will *not* be inferred from the sex of the individuals possessing the parental strands, even when the reproductive mode is essentially clonal from a single parent, since such inference would be ambiguous in the general case. Similarly, the offspring is considered to have no parents for the purposes of pedigree tracking, since there may be more than two "parents" in the general case. When modeling the X or Y, strand1 and strand2 must be X genomes (or NULL), and strand3 and strand4 must both be X genomes or both be Y genomes (or NULL).

These semantics allow several uses for addRecombinant(). When all strands are non-NULL, it is similar to addCrossed() except that the recombination breakpoints are specified explicitly, allowing very precise offspring generation without having to override SLiM's breakpoint generation with a recombination() callback. When only strand1 and strand3 are supplied, it is very similar to addCloned(), creating a clonal offspring, except that the two parental genomes need not belong to the same individual (whatever that might mean biologically). Supplying only strand1 is useful for modeling clonally reproducing haploids; the second genome of every offspring will be kept empty and will not receive new mutations. For a model of clonally reproducing haploids that undergo horizontal gene transfer (HGT), supplying only strand1 and strand2 will allow HGT from strand2 to replace segments of an otherwise clonal copy of strand1, while the second genome of the generated offspring will again be kept empty; this could be useful for modeling bacterial conjugation, for example. Other variations are also possible.

Note that this method is only for use in nonWF models. See addCrossed() for further general notes on the addition of new offspring individuals.

`– (No<Individual>$)addSelfed(object<Individual>$ parent)`

Generates a new offspring individual from the given parent by selfing, queues it for addition to the target subpopulation, and returns it. The new offspring will not be visible as a member of the target subpopulation until the end of the offspring generation life cycle stage. The subpopulation of parent will be used to locate applicable recombination() and modifyChild() callbacks governing the generation of the offspring individual.

Since selfing requires that `parent` act as a source of both a male and a female gamete, this method may be called only in hermaphroditic models; calling it in sexual models will result in an error. This method represents a non-incidental selfing event, so the `preventIncidentalSelfing` flag of `initializeSLiMOptions()` has no effect on this method (in contrast to the behavior of `addCrossed()`, where selfing is assumed to be incidental).

Note that this method is only for use in nonWF models. See `addCrossed()` for further general notes on the addition of new offspring individuals.

– `(float)cachedFitness(Ni indices)`

The fitness values calculated for the individuals at the indices given are returned. If `NULL` is passed, fitness values for all individuals in the subpopulation are returned. The fitness values returned are cached values; `fitness()` callbacks are therefore not called as a side effect of this method. It is always an error to call `cachedFitness()` from inside a `fitness()` callback, since fitness values are in the middle of being set up. In WF models, it is also an error to call `cachedFitness()` from a `late()` event, because fitness values for the new offspring generation have not yet been calculated and are undefined. In nonWF models, the population may be a mixture of new and old individuals, so instead, `NAN` will be returned as the fitness of any new individuals whose fitness has not yet been calculated. When new subpopulations are first created with `addSubpop()` or `addSubpopSplit()`, the fitness of all of the newly created individuals is considered to be `1.0` until fitness values are recalculated.

– `(void)configureDisplay([Nf center = NULL], [Nf$ scale = NULL],`
  `[Ns$ color = NULL])`

This method customizes the display of the subpopulation in SLiMgui's Population Visualization graph. When this method is called by a model running outside SLiMgui, it will do nothing except type-checking and bounds-checking its arguments. When called by a model running in SLiMgui, the position, size, and color of the subpopulation's displayed circle can be controlled as specified below.

The `center` parameter sets the coordinates of the center of the subpopulation's displayed circle; it must be a `float` vector of length two, such that `center[0]` provides the *x*-coordinate and `center[1]` provides the *y*-coordinate. The square central area of the Population Visualization occupies scaled coordinates in [0,1] for both *x* and *y*, so the values in `center` must be within those bounds. If a value of `NULL` is provided, SLiMgui's default center will be used (which currently arranges subpopulations in a circle).

The `scale` parameter sets a scaling factor to be applied to the radius of the subpopulation's displayed circle. The default radius used by SLiMgui is a function of the subpopulation's number of individuals; this default radius is then multiplied by `scale`. If a value of `NULL` is provided, the default radius will be used; this is equivalent to supplying a `scale` of `1.0`. Typically the same `scale` value should be used by all subpopulations, to scale all of their circles up or down uniformly, but that is not required.

The `color` parameter sets the color to be used for the displayed subpopulation's circle. Colors may be specified by name, or with hexadecimal RGB values of the form `"#RRGGBB"` (see the Eidos manual). If `color` is `NULL` or the empty string, `""`, SLiMgui's default (fitness-based) color will be used.

– `(void)defineSpatialMap(string$ name, string$ spatiality, Ni gridSize,`
  `float values, [logical$ interpolate = F], [Nf valueRange = NULL],`
  `[Ns colors = NULL])`

Defines a spatial map for the subpopulation. The map will henceforth be identified by `name`. The map uses the spatial dimensions referenced by spatiality, which must be a subset of the dimensions defined for the simulation in `initializeSLiMOptions()`. Spatiality `"x"` is permitted for dimensionality `"x"`; spatiality `"x"`, `"y"`, or `"xy"` for dimensionality `"xy"`; and spatiality `"x"`, `"y"`, `"z"`, `"xy"`, `"yz"`, `"xz"`, or `"xyz"` for dimensionality `"xyz"`. The spatial map is defined by a grid of values of a size specified by `gridSize`, which must have one value per spatial dimension (or `gridSize` may be `NULL`; see below); for a spatiality of `"xz"`, for example, `gridSize` must be of length `2`, specifying the size of the values grid in the *x* and *z* dimensions. The parameter `values` then gives the values of the grid; it must be of length equal to the product of the `gridSize` elements, and specifies values varying first (i.e., fastest) in the *x* dimension, then in *y*, then in *z*.

Beginning in SLiM 2.6, the `values` parameter may be a matrix/array with the number of dimensions appropriate for the declared spatiality of the map; for example, a map with spatiality `"xy"` would require a (two-dimensional) matrix, whereas a map with spatiality of `"xyz"` would require a three-dimensional array. (See the Eidos manual for discussion of matrices and arrays.) If a matrix/array argument is supplied for `values`, `gridSize` must either be `NULL`, or (for backward compatibility) may match the dimensions of `values` as they would be given by `dim(values)`. The data in `values` is interpreted just as is described above for the vector case: varying first in *x*, then in *y*, then in *z*. BEWARE: since the values in Eidos matrices and arrays are stored in column-first order (following the convention established by R), this means that for a map with spatiality `"xy"` each column of the `values` matrix will provide map data as *x* varies and *y* remains constant. This will be confusing if you think of matrix columns as being "*x*" and matrix rows as being "*y*", so try not to think that way; the opposite is true. This behavior is actually simple, self-consistent, and backward-compatible; if you before created a spatial map with a vector `values` before and a `gridSize` of `c(x, y)` specifying the dimensions of that vector, you can now supply `matrix(values, nrow=x)` for `values` to get exactly the same spatial map, and you can still supply the same value of `c(x, y)` for `gridSize` if you wish (or you may supply `NULL`). If, however, you are looking at a matrix as printed in the Eidos console, and want that matrix to be used as a spatial map in SLiM in the same orientation, you should use the transpose of the matrix, as supplied by the `t()` function. Actually, since matrices are printed in the console with each successive row having a *larger* index, whereas in Cartesian (*x*, *y*) coordinates *y*-values increase as you go *upward*, you may also wish to reverse the order of rows in your matrix prior to transposing (or the order of columns after transposing), with an expression such as `t(map[(nrow(map)-1):0,])`, in order to make the spatial map display in SLiMgui as you expect (since SLiMgui displays everything in Cartesian coordinates). Apologies if this is confusing; it would be nice if matrix notation, programming languages, and Descartes all agreed on such things, but they do not, so be very careful that your spatial maps are oriented as you wish them to be!

Moving on to the other parameters of `defineSpatialMap()`: if `interpolate` is `F`, values across the spatial map are not interpolated; the value at a given point is equal to the nearest value defined by the grid of values specified. If `interpolate` is `T`, values across the spatial map will be interpolated (using linear, bilinear, or trilinear interpolation as appropriate) to produce spatially continuous variation in values. In either case, the corners of the value grid are exactly aligned with the corners of the spatial boundaries of the subpopulation as specified by `setSpatialBoundary()`, and the value grid is then stretched across the spatial extent of the subpopulation in such a manner as to produce equal spacing between the values along each dimension. The setting of `interpolation` only affects how values between these grid points are calculated: by nearest-neighbor, or by linear interpolation. Interpolation of spatial maps with periodic boundaries is not handled specially; to ensure that the edges of a periodic spatial map join smoothly, simply ensure that the grid values at the edges of the map are identical, since they will be coincident after periodic wrapping.

The `valueRange` and `colors` parameters travel together; either both are unspecified, or both are specified. They control how map values will be transformed into colors, by SLiMgui and by the `spatialMapColor()` method. The `valueRange` parameter establishes the color-mapped range of spatial map values, as a vector of length two specifying a minimum and maximum; this does not need to match the actual range of values in the map. The `colors` parameter then establishes the corresponding colors for values within the interval defined by `valueRange`: values less than or equal to `valueRange[0]` will map to `colors[0]`, values greater than or equal to `valueRange[1]` will map to the last `colors` value, and intermediate values will shade continuously through the specified vector of colors, with interpolation between adjacent colors to produce a continuous spectrum. This is much simpler than it sounds in this description; see the recipes in chapter 14 for an illustration of its use.

Note that at present, SLiMgui will only display spatial maps of spatiality `"x"`, `"y"`, or `"xy"`; the color-mapping parameters will simply be ignored by SLiMgui for other spatiality values (even if the spatiality is a superset of these values; SLiMgui will not attempt to display an `"xyz"` spatial map, for example, since it has no way to choose which 2D slice through the *xyz* space it ought to display). The `spatialMapColor()` method will return translated color strings for any spatial map, however, even if SLiMgui is unable to display the spatial map. If there are multiple spatial maps with color-mapping parameters defined, SLiMgui will choose just one for display; it will prefer an `"xy"` map if one is available, but beyond that heuristic its choice will be arbitrary.

– `(+)getValue(string$ key)`

Returns the value previously set for the dictionary entry identifier `key` using `setValue()`, or `NULL` if no value has been set. This dictionary-style functionality is actually provided by the superclass of `Subpopulation`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

– `(void)outputMSSample(integer$ sampleSize, [logical$ replace = T], [string$ requestedSex = "*"], [Ns$ filePath = NULL], [logical$ append = F], [logical$ filterMonomorphic = F])`

Output a random sample from the subpopulation in MS format (see section 23.2.2 for output format details). Positions in the output will span the interval [0,1]. A sample of genomes (not entire individuals, note) of size `sampleSize` from the subpopulation will be output. The sample may be done either with or without replacement, as specified by `replace`; the default is to sample with replacement. A particular sex of individuals may be requested for the sample, for simulations in which sex is enabled, by passing `"M"` or `"F"` for `requestedSex`; passing `"*"`, the default, indicates that genomes from individuals should be selected randomly, without respect to sex. If the sampling options provided by this method are not adequate, see the `outputMS()` method of `Genome` for a more flexible low-level option.

If the optional parameter `filePath` is `NULL` (the default), output will be sent to Eidos's output stream (see section 4.2.1). Otherwise, output will be sent to the filesystem path specified by `filePath`, overwriting that file if `append` if `F`, or appending to the end of it if `append` is `T`.

If `filterMonomorphic` is `F` (the default), all mutations that are present in the sample will be included in the output. This means that some mutations may be included that are actually monomorphic within the sample (i.e., that exist in *every* sampled genome, and are thus apparently fixed). These may be filtered out with `filterMonomorphic = T` if desired; note that this option means that some mutations that do exist in the sampled genomes might not be included in the output, simply because they exist in every sampled genome.

See `outputSample()` and `outputVCFSample()` for other output formats. Output is generally done in a `late()` event, so that the output reflects the state of the simulation at the end of a generation.

– `(void)outputSample(integer$ sampleSize, [logical$ replace = T], [string$ requestedSex = "*"], [Ns$ filePath = NULL], [logical$ append = F])`

Output a random sample from the subpopulation in SLiM's native format (see section 23.2.1 for output format details). A sample of genomes (not entire individuals, note) of size `sampleSize` from the subpopulation will be output. The sample may be done either with or without replacement, as specified by `replace`; the default is to sample with replacement. A particular sex of individuals may be requested for the sample, for simulations in which sex is enabled, by passing `"M"` or `"F"` for `requestedSex`; passing `"*"`, the default, indicates that genomes from individuals should be selected randomly, without respect to sex. If the sampling options provided by this method are not adequate, see the `output()` method of `Genome` for a more flexible low-level option.

If the optional parameter `filePath` is `NULL` (the default), output will be sent to Eidos's output stream (see section 4.2.1). Otherwise, output will be sent to the filesystem path specified by `filePath`, overwriting that file if `append` if `F`, or appending to the end of it if `append` is `T`.

See `outputMSSample()` and `outputVCFSample()` for other output formats. Output is generally done in a `late()` event, so that the output reflects the state of the simulation at the end of a generation.

– `(void)outputVCFSample(integer$ sampleSize, [logical$ replace = T],`
`[string$ requestedSex = "*"], [logical$ outputMultiallelics = T],`
`[Ns$ filePath = NULL], [logical$ append = F])`

Output a random sample from the subpopulation in VCF format (see section 23.2.3 for output format details). A sample of individuals (not genomes, note – unlike the `outputSample()` and `outputMSSample()` methods) of size `sampleSize` from the subpopulation will be output. The sample may be done either with or without replacement, as specified by `replace`; the default is to sample with replacement. A particular sex of individuals may be requested for the sample, for simulations in which sex is enabled, by passing `"M"` or `"F"` for `requestedSex`; passing `"*"`, the default, indicates that genomes from individuals should be selected randomly, without respect to sex. If the sampling options provided by this method are not adequate, see the `outputVCF()` method of `Genome` for a more flexible low-level option.

In SLiM, it is often possible for a single individual to have multiple mutations at a given base position. Because the VCF format is an explicit-nucleotide format, this property of SLiM does not fit well into VCF. Since there are only four possible nucleotides at a given base position in VCF, at most one "reference" state and three "alternate" states could be represented at that base position. SLiM, on the other hand, can represent any number of alternative possibilities at a given base; in general, if *N* different mutations are segregating at a given position, there are 2^N different allelic states at that position in SLiM. For this reason, SLiM does not attempt to represent multiple mutations at a single site as being alternative alleles in a single output line, as is typical in VCF format. Instead, SLiM produces a separate line of VCF output for each segregating mutation at a given position. SLiM always declares base positions as having a "reference base" of `A` (representing the state in individuals that do not carry a given mutation) and an "alternate base" of `T` (representing the state in individuals that do carry the given mutation). Multiallelic positions will thus produce VCF output showing multiple `A`-to-`T` changes at the same position, possessed by different but possibly overlapping sets of individuals. Many programs that process VCF output may not behave correctly with this style of output. SLiM therefore provides a choice, using the `outputMultiallelics` flag; if that flag is `T` (the default), SLiM will produce multiple lines of output for multiallelic base positions, but will mark those lines with a `MULTIALLELIC` flag in the `INFO` field of the VCF output so that those lines can be filtered or processed in a special manner. If `outputMultiallelics` is `F`, on the other hand, SLiM will completely suppress output of all mutations at multiallelic sites – often the simplest option, if doing so does not lead to bias in the subsequent analysis. This flag has no effect upon the output of sites with only a single mutation present. Assessment of whether a site is multiallelic is done only within the sample; segregating mutations that are not part of the sample are ignored.

If the optional parameter `filePath` is `NULL` (the default), output will be sent to Eidos's output stream (see section 4.2.1). Otherwise, output will be sent to the filesystem path specified by `filePath`, overwriting that file if `append` if `F`, or appending to the end of it if `append` is `T`.

See `outputMSSample()` and `outputSample()` for other output formats. Output is generally done in a `late()` event, so that the output reflects the state of the simulation at the end of a generation.

– `(logical)pointInBounds(float point)`

Returns `T` if `point` is inside the spatial boundaries of the subpopulation, `F` otherwise. For example, for a simulation with `"xy"` dimensionality, if `point` contains exactly two values constituting an (*x*,*y*) point, the result will be `T` if and only if `((point[0]>=x0) & (point[0]<=x1) & (point[1]>=y0) & (point[1]<=y1))` given spatial bounds `(x0, y0, x1, y1)`. This method is useful for implementing absorbing or reprising boundary conditions. This may only be called in simulations for which continuous space has been enabled with `initializeSLiMOptions()`.

The length of `point` must be an exact multiple of the dimensionality of the simulation; in other words, `point` may contain values comprising more than one point. In this case, a `logical` vector will be returned in which each element is `T` if the corresponding point in `point` is inside the spatial boundaries of the subpopulation, `F` otherwise.

– `(float)pointPeriodic(float point)`

Returns a revised version of `point` that has been brought inside the periodic spatial boundaries of the subpopulation (as specified by the `periodicity` parameter of `initializeSLiMOptions()`) by wrapping around periodic spatial boundaries. In brief, if a coordinate of `point` lies beyond a periodic spatial boundary, that coordinate is wrapped around the boundary, so that it lies inside the spatial extent by the same magnitude that it previously lay outside, but on the opposite side of the space; in effect, the two edges of the periodic spatial boundary are seamlessly joined. This is done iteratively until all coordinates lie inside the subpopulation's periodic boundaries. Note that non-periodic spatial boundaries are not enforced by this method; they should be enforced using `pointReflected()`, `pointStopped()`, or some other means of enforcing boundary constraints (which can be used after `pointPeriodic()` to bring the remaining coordinates into bounds; coordinates already brought into bounds by `pointPeriodic()` will be unaffected by those calls). This method is useful for implementing periodic boundary conditions. This may only be called in simulations for which continuous space and at least one periodic spatial dimension have been enabled with `initializeSLiMOptions()`.

The length of `point` must be an exact multiple of the dimensionality of the simulation; in other words, `point` may contain values comprising more than one point. In this case, each point will be processed as described above and a new vector containing all of the processed points will be returned.

– `(float)pointReflected(float point)`

Returns a revised version of `point` that has been brought inside the spatial boundaries of the subpopulation by reflection. In brief, if a coordinate of `point` lies beyond a spatial boundary, that coordinate is reflected across the boundary, so that it lies inside the boundary by the same magnitude that it previously lay outside the boundary. This is done iteratively until all coordinates lie inside the subpopulation's boundaries. This method is useful for implementing reflecting boundary conditions. This may only be called in simulations for which continuous space has been enabled with `initializeSLiMOptions()`.

The length of `point` must be an exact multiple of the dimensionality of the simulation; in other words, `point` may contain values comprising more than one point. In this case, each point will be processed as described above and a new vector containing all of the processed points will be returned.

– `(float)pointStopped(float point)`

Returns a revised version of `point` that has been brought inside the spatial boundaries of the subpopulation by clamping. In brief, if a coordinate of `point` lies beyond a spatial boundary, that coordinate is set to exactly the position of the boundary, so that it lies on the edge of the spatial boundary. This method is useful for implementing stopping boundary conditions. This may only be called in simulations for which continuous space has been enabled with `initializeSLiMOptions()`.

The length of `point` must be an exact multiple of the dimensionality of the simulation; in other words, `point` may contain values comprising more than one point. In this case, each point will be processed as described above and a new vector containing all of the processed points will be returned.

– `(float)pointUniform([integer$ n = 1])`

Returns a new point (or points, for `n` > 1) generated from uniform draws for each coordinate, within the spatial boundaries of the subpopulation. The returned vector will contain `n` points, each comprised of a number of coordinates equal to the dimensionality of the simulation, so it will be of total length `n`*dimensionality. This may only be called in simulations for which continuous space has been enabled with `initializeSLiMOptions()`.

– `(void)removeSubpopulation(void)`

Removes this subpopulation from the model. The subpopulation is immediately removed from the list of active subpopulations, and the symbol representing the subpopulation is undefined. The subpopulation object itself remains unchanged until children are next generated (at which point it is deallocated), but it is no longer part of the simulation and should not be used.

Note that this method is only for use in nonWF models, in which there is a distinction between a subpopulation being empty and a subpopulation being removed from the simulation; an empty subpopulation may be re-colonized by migrants, whereas as a removed subpopulation no longer exists at all. WF models do not make this distinction; when a subpopulation is empty it is automatically removed. WF models should therefore call `setSubpopulationSize(0)` instead of this method; `setSubpopulationSize()` is the standard way for WF models to change the subpopulation size, including to a size of `0`.

```
– (object<Individual>)sampleIndividuals(integer$ size, [logical$ replace = F],
    [No<Individual>$ exclude = NULL], [Ns$ sex = NULL],[Ni$ tag = NULL],
    [Ni$ minAge = NULL], [Ni$ maxAge = NULL], [Nl$ migrant = NULL])
```

Returns a vector of individuals, of size less than or equal to parameter `size`, sampled from the individuals in the target subpopulation. Sampling is done without replacement if `replace` is `F` (the default), or with replacement if `replace` is `T`. The remaining parameters specify constraints upon the pool of individuals that will be considered candidates for the sampling. Parameter `exclude`, if non-`NULL`, may specify a specific individual that should not be considered a candidate (typically the focal individual in some operation). Parameter `sex`, if non-`NULL`, may specify a sex (`"M"` or `"F"`) for the individuals to be drawn, in sexual models. Parameter `tag`, if non-`NULL`, may specify a tag value for the individuals to be drawn; only individuals whose `tag` property matches this value will be candidates. Parameters `minAge` and `maxAge`, if non-`NULL`, may specify a minimum or maximum age for the individuals to be drawn, in nonWF models. Parameter `migrant`, if non-`NULL`, may specify a required value for the `migrant` property of the individuals to be drawn (so `T` will require that individuals be migrants, `F` will require that they not be). If the candidate pool is smaller than the requested sample size, all eligible candidates will be returned (in randomized order); the result will be a zero-length vector if no eligible candidates exist (unlike `sample()`).

This method is similar to getting the `individuals` property of the subpopulation, using operator `[]` to select only individuals with the desired properties, and then using `sample()` to sample from that candidate pool. However, besides being much simpler than the equivalent Eidos code, it is also much faster, and it does not fail if less than the full sample size is available. See `subsetIndividuals()` for a similar method that returns a full subset, rather than a sample.

```
– (void)setCloningRate(numeric rate)
```

Set the cloning rate of this subpopulation. The rate is changed to `rate`, which should be between 0.0 and 1.0, inclusive. Clonal reproduction can be enabled in both non-sexual (i.e. hermaphroditic) and sexual simulations. In non-sexual simulations, `rate` must be a singleton value representing the overall clonal reproduction rate for the subpopulation. In sexual simulations, `rate` may be either a singleton (specifying the clonal reproduction rate for both sexes) or a vector containing two numeric values (the female and male cloning rates specified separately, at indices `0` and `1` respectively). During mating and offspring generation, the probability that any given offspring individual will be generated by cloning – by asexual reproduction without gametes or meiosis – will be equal to the cloning rate (for its sex, in sexual simulations) set in the parental (not the offspring!) subpopulation.

```
– (void)setMigrationRates(io<Subpopulation> sourceSubpops, numeric rates)
```

Set the migration rates to this subpopulation from the subpopulations in `sourceSubpops` to the corresponding rates specified in `rates`; in other words, `rates` gives the expected fractions of the children in this subpopulation that will subsequently be generated from parents in the subpopulations `sourceSubpops` (see section 19.2.1). This method will only set the migration fractions from the subpopulations given; migration rates from other subpopulations will be left unchanged (explicitly set a zero rate to turn off migration from a given subpopulation). The type of `sourceSubpops` may be either `integer`, specifying subpopulations by identifier, or `object`, specifying subpopulations directly.

```
– (void)setSelfingRate(numeric$ rate)
```

Set the selfing rate of this subpopulation. The rate is changed to `rate`, which should be between 0.0 and 1.0, inclusive. Selfing can only be enabled in non-sexual (i.e. hermaphroditic) simulations.

During mating and offspring generation, the probability that any given offspring individual will be generated by selfing – by self-fertilization via gametes produced by meiosis by a single parent – will be equal to the selfing rate set in the parental (not the offspring!) subpopulation.

– `(void)setSexRatio(float$ sexRatio)`

Set the sex ratio of this subpopulation to `sexRatio`. As defined in SLiM, this is actually the fraction of the subpopulation that is male; in other words, the M:(M+F) ratio. This will take effect when children are next generated; it does not change the current subpopulation state. Unlike the selfing rate, the cloning rate, and migration rates, the sex ratio is deterministic: SLiM will generate offspring that exactly satisfy the requested sex ratio (within integer roundoff limits). See section 19.2.1 for further details.

– `(void)setSpatialBounds(float bounds)`

Set the spatial boundaries of the subpopulation to `bounds`. This method may be called only for simulations in which continuous space has been enabled with `initializeSLiMOptions()`. The length of `bounds` must be double the spatial dimensionality, so that it supplies both minimum and maximum values for each coordinate. More specifically, for a dimensionality of `"x"`, `bounds` should supply `(x0, x1)` values; for dimensionality `"xy"` it should supply `(x0, y0, x1, y1)` values; and for dimensionality `"xyz"` it should supply `(x0, y0, z0, x1, y1, z1)` (in that order). These boundaries will be used by SLiMgui to calibrate the display of the subpopulation, and will be used by methods such as `pointInBounds()`, `pointReflected()`, `pointStopped()`, and `pointUniform()`. The default spatial boundaries for all subpopulations span the interval `[0,1]` in each dimension. Spatial dimensions that are periodic (as established with the `periodicity` parameter to `initializeSLiMOptions()`) must have a minimum coordinate value of `0.0` (a restriction that allows the handling of periodicity to be somewhat more efficient). The current spatial bounds for the subpopulation may be obtained through the `spatialBounds` property.

– `(void)setSubpopulationSize(integer$ size)`

Set the size of this subpopulation to `size` individuals. This will take effect when children are next generated; it does not change the current subpopulation state. Setting a subpopulation to a size of 0 does have some immediate effects that serve to disconnect it from the simulation: the subpopulation is removed from the list of active subpopulations, the subpopulation is removed as a source of migration for all other subpopulations, and the symbol representing the subpopulation is undefined. In this case, the subpopulation itself remains unchanged until children are next generated (at which point it is deallocated), but it is no longer part of the simulation and should not be used.

– `(void)setValue(string$ key, + value)`

Sets a value for the dictionary entry identifier `key`. The value, which may be of any type other than `object`, can be fetched later using `getValue()`. This dictionary-style functionality is actually provided by the superclass of `Subpopulation`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

– `(string)spatialMapColor(string$ name, float value)`

Looks up the spatial map indicated by `name`, and uses its color-translation machinery (as defined by the `valueRange` and `colors` parameters to `defineSpatialMap()`) to translate each element of `value` into a corresponding color string. If the spatial map does not have color-translation capabilities, an error will result. See the documentation for `defineSpatialMap()` for information regarding the details of color translation. See the Eidos manual for further information on color strings.

– `(float$)spatialMapValue(string$ name, float point)`

Looks up the spatial map indicated by `name`, and uses its mapping machinery (as defined by the `gridSize`, `values`, and `interpolate` parameters to `defineSpatialMap()`) to translate the coordinates of `point` into a corresponding map value. The length of `point` must be equal to the spatiality of the spatial map; in other words, for a spatial map with spatiality `"xz"`, `point` must be of length `2`, specifying the *x* and *z* coordinates of the point to be evaluated. Interpolation will automatically be used if it was enabled for the spatial map. Point coordinates are clamped into the range defined by the spatial boundaries, even if the spatial boundaries are periodic; use `pointPeriodic()` to wrap the point coordinates first if desired. See the documentation for `defineSpatialMap()` for information regarding the details of value mapping.

`– (object<Individual>)subsetIndividuals([No<Individual>$ exclude = NULL], [Ns$ sex = NULL],[Ni$ tag = NULL], [Ni$ minAge = NULL], [Ni$ maxAge = NULL], [Nl$ migrant = NULL])`

Returns a vector of individuals subset from the individuals in the target subpopulation. The parameters specify constraints upon the subset of individuals that will be returned. Parameter `exclude`, if non-`NULL`, may specify a specific individual that should not be included (typically the focal individual in some operation). Parameter `sex`, if non-`NULL`, may specify a sex (`"M"` or `"F"`) for the individuals to be returned, in sexual models. Parameter `tag`, if non-`NULL`, may specify a tag value for the individuals to be returned; only individuals whose `tag` property matches this value will be returned. Parameters `minAge` and `maxAge`, if non-`NULL`, may specify a minimum or maximum age for the individuals to be returned, in nonWF models. Parameter `migrant`, if non-`NULL`, may specify a required value for the `migrant` property of the individuals to be returned (so `T` will require that individuals be migrants, `F` will require that they not be).

This method is shorthand for getting the `individuals` property of the subpopulation, and then using operator `[]` to select only individuals with the desired properties; besides being much simpler than the equivalent Eidos code, it is also much faster. See `sampleIndividuals()` for a similar method that returns a sample taken from a chosen subset of individuals.

`– (void)takeMigrants(object<Individual> migrants)`

Immediately moves the individuals in `migrants` to the target subpopulation (removing them from their previous subpopulation). Individuals in `migrants` that are already in the target subpopulation are unaffected. Note that the indices and order of individuals and genomes in both the target and source subpopulations will change unpredictably as a side effect of this method.

Note that this method is only for use in nonWF models, in which migration is managed manually by the model script. In WF models, migration is managed automatically by the SLiM core based upon the migration rates set for each subpopulation with `setMigrationRates()`.

21.14 Class Substitution

This class represents a mutation that has been fixed; Mutation objects are converted to Substitution objects upon fixation. Its properties are thus very similar to those of Mutation. Section 1.5.2 presents an overview of the conceptual role of this class.

Although `Substitution` has a `tag` property, like most SLiM classes, an associated value for `Substitution` objects may also be kept in the `subpopID` property (see section 21.8).

21.14.1 `Substitution` properties

`id => (integer$)`

The identifier for this mutation. Each mutation created during a run receives an immutable identifier that will be unique across the duration of the run, and that identifier is carried over to the `Substitution` object when the mutation fixes.

`fixationGeneration => (integer$)`

The generation in which this mutation fixed.

`mutationType => (object<MutationType>$)`

The `MutationType` from which this mutation was drawn.

`originGeneration => (integer$)`

The generation in which this mutation arose.

`position => (integer$)`

The position in the chromosome of this mutation.

`selectionCoeff => (float$)`

The selection coefficient of the mutation, drawn from the distribution of fitness effects of its `MutationType`.

`subpopID <–> (integer$)`

The identifier of the subpopulation in which this mutation arose. This value is carried over from the `Mutation` object directly; if a "tag" value was used in the `Mutation` object (see section 21.8.1), that value will carry over to the corresponding `Substitution` object. The `subpopID` in `Substitution` is a read-write property to allow it to be used as a "tag" in the same way, if the origin subpopulation identifier is not needed.

`tag <–> (integer$)`

A user-defined `integer` value. The value of `tag` is carried over automatically from the original `Mutation` object. Apart from that, the value of `tag` is not used by SLiM; it is free for you to use.

21.14.2 `Substitution` methods

Since `Substitution` objects represent fixation events that occurred in the past, they are relatively immutable. However, since it may be useful to attach (possibly dynamic) state to substitutions, their `tag` and `subpopID` properties are mutable, and they also provide the same `getValue()` / `setValue()` functionality as `Mutation`. Values set on a `Mutation` object will carry over to the corresponding `Substitution` object automatically upon fixation.

`– (+)getValue(string$ key)`

Returns the value previously set for the dictionary entry identifier `key` using `setValue()`, or `NULL` if no value has been set. This dictionary-style functionality is actually provided by the superclass of `Substitution`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

`– (void)setValue(string$ key, + value)`

Sets a value for the dictionary entry identifier `key`. The value, which may be of any type other than `object`, can be fetched later using `getValue()`. This dictionary-style functionality is actually provided by the superclass of `Substitution`, `SLiMEidosDictionary`, although that fact is not presently visible in Eidos since superclasses are not introspectable.

22. Writing Eidos events and callbacks

In the preceding recipes, we have seen many examples of Eidos events and callbacks, but we have not systematically described their syntax and semantics. Eidos events and callbacks are typically used in SLiM simulations by defining them in the SLiM input file; they can also be registered with the simulation dynamically at runtime (see sections 10.5.3 and 16.4, for example).

There are two main ways to use Eidos in the input file. One way is by defining an *Eidos event*, a block of Eidos code that is executed during each generation. The other way is by defining an *Eidos callback*, a block of code that is called by SLiM in specific circumstances to extend the functionality of SLiM in particular areas. One type of Eidos callback, the `initialize()` callback, was described in section 21.1. The sections below will detail the remaining possibilities.

22.1 Defining Eidos events

An Eidos event is a block of Eidos code that is executed every generation, within a generation range, to perform a desired task. The syntax of an Eidos event declaration looks like one of these:

```
[id] [gen1 [: gen2]] { ... }
[id] [gen1 [: gen2]] early() { ... }
[id] [gen1 [: gen2]] late() { ... }
```

The first two declarations are exactly equivalent, and declare an `early()` event that executes at the beginning of the generation cycle; the `early()` designation is therefore optional. The third declaration declares a `late()` event that executes near the end of the generation cycle (see chapter 19 for a discussion of the stages of the generation cycle and the differences between these two types of events).

The `id` is an optional identifier like `s1` (or more generally, `sX`, where `X` is an integer greater than or equal to `0`) that defines an identifier that can be used to refer to the script block. In most situations it can be omitted, in which case the id is implicitly defined as `-1`, a placeholder value that essentially represents the lack of an identifier value. Supplying an `id` is only useful if you wish to manipulate your script blocks programmatically (see section 22.8).

Then comes a generation or a range of generations, and then a block of Eidos code enclosed in braces to form a compound statement. A trivial example might look like this:

```
1000:5000 {
    p1.size = 1000 * sin(sim.generation / 100.0);
}
```

This would set the size of subpopulation `p1` to the result of an expression based on the `sin()` function, resulting in a fluctuating subpopulation size. This idea is further developed in the recipe in section 5.1.4; here, the point is that the Eidos code in the braces `{}` is executed near the end of every generation in the specified range of generations. In this case, the generation range is `1000` to `5000`, and so the Eidos event will be executed 4001 times. A range of generations can be given, as in the example above, or a single generation can be given with a single integer:

```
100 late() {
    print("Finished generation 100!");
}
```

In fact, you can omit specifying a generation altogether, in which case the Eidos event runs every generation. However, since it takes a little time to set up the Eidos interpreter and interpret a script, it is advisable to use the narrowest range of generations possible.

The generations specified for a Eidos event block can be any positive integer. All scripts that apply to a given time point will be run in the order in which they are given; scripts specified higher in the input file will run before those specified lower. Sometimes it is desirable to have a script block execute in a generation which is not fixed, but instead depends upon some parameter, defined constant, or calculation; this may be achieved by rescheduling the script block with the `SLiMSim` method `rescheduleScriptBlock()` (see section 17.2 for an example).

When Eidos events are executed, several global variables are defined by SLiM for use by the Eidos code. These have been mentioned in previous sections, but here is a summary:

`sim`	A `SLiMSim` object representing the current SLiM simulation
`g1, ...`	`GenomicElementType` objects representing the genomic element types defined
`i1, ...`	`InteractionType` objects representing the interaction types defined
`m1, ...`	`MutationType` objects representing the mutation types defined
`p1, ...`	`Subpopulation` objects representing the subpopulations that exist
`s1, ...`	`SLiMEidosBlock` objects representing the named events and callbacks defined
`self`	A `SLiMEidosBlock` object representing the script block currently executing

Note that the `sim` global is *not* available in `initialize()` callbacks, since the simulation has not yet been initialized (see section 21.1). Similarly, the globals for subpopulations, mutation types, and genomic element types are only available after the point at which those objects have been defined by an `initialize()` callback.

22.2 Defining mutation fitness with a `fitness()` callback

An Eidos callback is a block of Eidos code that is called by SLiM in specific circumstances, to allow the customization of particular actions taken by SLiM in running a simulation. Five types of callbacks are presently supported (in addition to the `initialize()` callbacks described in section 21.1): `fitness()` callbacks, discussed here, and `mateChoice()`, `modifyChild()`, `recombination()`, and `interaction()` callbacks, discussed in the following sections.

A `fitness()` callback is called by SLiM when it is determining the fitness effect of a mutation carried by an individual. Normally, the fitness effect of a mutation is determined by the selection coefficient of the mutation and the dominance coefficient of the mutation (the latter used only if the individual is heterozygous for the mutation). More specifically, the standard calculation for the fitness effect of a mutation takes one of two forms. If the individual is homozygous, then

$$w = w * (1.0 + \text{selectionCoefficient}),$$

where w is the relative fitness of the individual carrying the mutation. This equation is also used if the chromosome being simulated has no homologue – when the Y sex chromosome is being simulated. If the individual is heterozygous, then the dominance coefficient enters the picture as

$$w = w * (1.0 + \text{dominanceCoeff} * \text{selectionCoeff}).$$

For simulations of autosomes, the dominance coefficient is defined by the mutation type; for simulations of X sex chromosomes, the mutation type's dominance coefficient is used for XX females that are heterozygous, whereas XY males that are "heterozygous" for the mutation because they possess only one X chromosome use a global dominance coefficient (see `initializeSex()`, section 21.1, and the `dominanceCoeffX` property of `SLiMSim`, section 21.12.1).

That is the standard behavior of SLiM, reviewed here to provide a conceptual baseline. Supplying a `fitness()` callback allows you to substitute any calculation you wish for the relative fitness effect of a mutation; the new relative fitness effect computation becomes

```
w = w * fitness()
```

where `fitness()` is the value returned by your callback. This value is a relative fitness value, so `1.0` is neutral, unlike the selection coefficient scale, where `0.0` is neutral; be careful with this distinction! Like Eidos events, `fitness()` callbacks are defined as script blocks in the input file, but they use a variation of the syntax for defining a Eidos event:

```
[id] [gen1 [: gen2]] fitness(<mut-type-id> [, <subpop-id>]) { ... }
```

For example, if the callback were defined as:

```
1000:2000 fitness(m2, p3) { 1.0; }
```

then a relative fitness of `1.0` (i.e. neutral) would be used for all mutations of mutation type `m2` in subpopulation `p3` from generation `1000` to generation `2000`. The very same mutations, if also present in individuals in other subpopulations, would preserve their normal selection coefficient and dominance coefficient in those other subpopulations; this callback would therefore establish spatial heterogeneity in selection, in which mutation type `m2` was neutral in subpopulation `p3` but under selection in other subpopulations, for the range of generations given (see the recipe in section 9.2 for a fuller explication of this idea).

In addition to the SLiM globals listed in section 22.1, a `fitness()` callback is supplied with some additional information passed through global variables:

`mut`	A Mutation object, the mutation whose relative fitness is being evaluated
`homozygous`	A value of `T` (the mutation is homozygous), `F` (heterozygous), or `NULL` (it is paired with a null chromosome, which can occur with sex chromosomes)
`relFitness`	The default relative fitness value calculated by SLiM
`individual`	The individual carrying this mutation (an object of class `Individual`)
`genome1`	One genome of the individual carrying this mutation
`genome2`	The other genome of that individual
`subpop`	The subpopulation in which that individual lives

These globals may be used in the `fitness()` callback to compute a fitness value. To implement the standard fitness functions used by SLiM for an autosomal simulation, for example, you could do something like this:

```
fitness(m1) {
    if (homozygous)
       return 1.0 + mut.selectionCoeff;
    else
       return 1.0 + mut.mutationType.dominanceCoeff * mut.selectionCoeff;
}
```

As mentioned above, a relative fitness of `1.0` is neutral (whereas a selection coefficient of `0.0` is neutral); the `1.0 +` in these calculations converts between the selection coefficient scale and the relative fitness scale, and is therefore essential. However, the `relFitness` global variable mentioned above would already contain this value, precomputed by SLiM, so you could simply return `relFitness` to get that behavior when you want it:

```
fitness(m1) {
    if (<conditions>)
       <custom fitness calculations...>;
    else
```

```
        return relFitness;
    }
```

This would return a modified fitness value in certain conditions, but would return the standard fitness value otherwise.

More than one `fitness()` callback may be defined to operate in the same generation. As with Eidos events, multiple callbacks will be called in the order in which they were defined in the input file. Furthermore, each callback will be given the `relFitness` value returned by the previous callback – so the value of `relFitness` is not necessarily the default value, in fact, but is the result of all previous `fitness()` callbacks for that individual in that generation. In this way, the effects of multiple callbacks can "stack".

In SLiM version 2.3 and later, it is possible to define *global* `fitness()` callbacks, which are applied exactly once to every individual (within a given subpopulation, if the `fitness()` callback is declared to be limited to one subpopulation, as usual). Global `fitness()` callbacks do not reference a particular mutation type, and are not called in reference to any specific mutation in the individual; instead, they provide an opportunity for the model script to define fitness effects that are independent of specific mutations (although their fitness effects may still depend upon some aggregate genetic state). For example, they are useful for defining the fitness effect of an individual's overall phenotype (perhaps determined by multiple loci, and perhaps by developmental noise, phenotypic plasticity, etc.), or for defining the fitness effects of behavioral interactions between individuals such as competition or altruism. A global `fitness()` callback is defined by giving `NULL` as the mutation type identifier in the callback's declaration. These callbacks will generally be called once per individual in each generation, in an order that is formally undefined, as described in detail in section 19.6. When a global `fitness()` callback is running, the `mut` and `homozygous` variables are defined to be `NULL` (since there is no focal mutation), and `relFitness` is defined to be `1.0`. The fitness effect for the callback is simply returned as a singleton `float` value, as usual. Examples of global `fitness()` callbacks can be found in the recipes of sections 13.1, 13.3, 13.10, 14.2, 14.4, and 14.5 (and perhaps others).

Beginning in SLiM 3.0, it is also possible to set the `fitnessScaling` property on a subpopulation to scale the fitness values of every individual in the subpopulation by the same constant amount, or to set the `fitnessScaling` property on an individual to scale the fitness value of that specific individual. These scaling factors are multiplied together with all other fitness effects for an individual to produce the individual's final fitness value. The `fitnessScaling` properties of `Subpopulation` and `Individual` can often provide similar functionality to `fitness(NULL)` callbacks with greater efficiency and simplicity. They are reset to `1.0` in every generation, immediately after fitness values are calculated, so they only need to be set when a value other than `1.0` is desired.

One caveat to be aware of is that `fitness()` callbacks are called at the end of each generation, just before the next generation begins. If you have a `fitness()` callback defined for generation `10`, for example, it will actually be called at the very end of generation `10`, after child generation has finished, after the new children have been promoted to be the next parental generation, and after `late()` events have been executed. The fitness values calculated will thus be used during generation `11`; the fitness values used in generation `10` were calculated at the end of generation `9`. (This is primarily so that SLiMgui, which refreshes its display in between generations, has computed fitness values at hand that it can use to display the new parental individuals in the proper colors.)

Many other possibilities can be implemented with a `fitness()` callback. For example, one could implement epistatic interactions by checking the genomes provided to see whether they contain the other mutations involved in the epistasis (section 9.3.1); one could implement negative frequency-dependent selection (balancing selection) by checking the frequency of the mutation in the subpopulation (section 9.4.1); one could implement a polygenic fitness calculation by counting how many mutations of a given mutation type were present in the genome of the individual (section 9.3.2); or one could implement spatial variation in the fitness of heterozygotes by varying the dominance coefficient depending upon the subpopulation (similar to section 9.2).

The `fitness()` callback mechanism is thus extremely powerful and flexible. However, since `fitness()` callbacks involve Eidos code being executed for the evaluation of fitness of every mutation of every individual (within the generation range, mutation type, and subpopulation specified), they can slow down a simulation considerably, so use them as sparingly as possible.

22.3 Defining mate choice with a `mateChoice()` callback

Normally, a SLiM simulation defines mate choice according to fitness; individuals of higher fitness are more likely to be chosen as mates. However, one might wish to simulate more complex mate-choice dynamics such as assortative or disassortative mating, mate search algorithms, and so forth. Such dynamics can be handled in SLiM with the `mateChoice()` callback mechanism.

A `mateChoice()` callback is established in the input file with a syntax very similar to that of `fitness()` callbacks (section 22.2):

```
[id] [gen1 [: gen2]] mateChoice([<subpop-id>]) { ... }
```

The only difference between the two is that the `mateChoice()` callback does not allow you to specify a mutation type to which the callback applies, since that makes no sense.

Note that if a subpopulation is given to which the `mateChoice()` callback is to apply, the callback is used for all matings that will generate a *child* in the stated subpopulation (as opposed to all matings of *parents* in the stated subpopulation); this distinction is important when migration causes children in one subpopulation to be generated by matings of parents in a different subpopulation.

When a `mateChoice()` callback is defined, the first parent in a mating is still chosen proportionally according to fitness (if you wish to influence that choice, you can use a `fitness()` callback; see section 22.2). In a sexual (rather than hermaphroditic) simulation, this will be the female parent; SLiM does not currently support males as the choosy sex. The second parent – the male parent, in a sexual simulation – will then be chosen based upon the results of the `mateChoice()` callback.

More specifically, the callback must return a vector of weights, one for each individual in the subpopulation; SLiM will then choose a parent with probability proportional to weight. The `mateChoice()` callback could therefore modify or replace the standard fitness-based weights depending upon some other criterion such as assortativeness. A singleton vector of type `Individual` may be returned instead of a weights vector to indicate that that specific individual has been chosen as the mate (beginning in SLiM 2.3); this could also be achieved by returned a vector of weights in which the chosen mate has a non-zero weight and all other weights are zero, but returning the chosen individual instead is much more efficient. A zero-length return vector – as generated by `float(0)`, for example – indicates that a suitable mate was not found; in that event, a new first parent will be drawn from the subpopulation. Finally, if the callback returns `NULL`, that signifies that SLiM should use the standard fitness-based weights to choose a mate; the `mateChoice()` callback did not wish to alter the standard behavior for the current mating (this is equivalent to returning the unmodified vector of weights, but returning `NULL` is much faster since it allows SLiM to drop into an optimized case). Apart from the special cases described above – a singleton `Individual`, `float(0)`, and `NULL` – the returned vector of weights must contain the same number of values as the size of the subpopulation, and all weights must be non-negative. Note that the vector of weights is not required to sum to `1`, however; SLiM will convert relative weights on any scale to probabilities for you.

If the sum of the returned weights vector is zero, SLiM treats it as meaning the same thing as a return of `float(0)` – a suitable mate could not be found, and a new first parent will thus be drawn. (This is a change in policy beginning in SLiM 2.3; prior to that, returning a vector of sum zero was considered a runtime error.) There is a subtle difference in semantics between this and a return of `float(0)`: returning `float(0)` immediately short-circuits mate choice for the current first parent, whereas returning a vector of zeros allows further applicable `mateChoice()` callbacks to be called, one of which might "rescue" the first parent by returning a non-zero weights vector or an individual. In most models this distinction is irrelevant, since chaining `mateChoice()` callbacks is uncommon (see section 22.8). When the choice is otherwise unimportant, returning `float(0)` will be handled more quickly by SLiM; but if a model is constructing a vector of weights anyway, checking for `sum(...) == 0` in order to return `float(0)` if the weights all happen to be zero is complicated and slow – which is why this policy was changed.

In addition to the SLiM globals listed in section 22.1, a `mateChoice()` callback is supplied with some additional information passed through global variables:

`individual`	The parent already chosen (the female, in sexual simulations)
`genome1`	One genome of the parent already chosen
`genome2`	The other genome of the parent already chosen
`subpop`	The subpopulation into which the offspring will be placed
`sourceSubpop`	The subpopulation from which the parents are being chosen
`weights`	The standard fitness-based weights for all individuals

If sex is enabled, the `mateChoice()` callback must ensure that the appropriate weights are zero and nonzero to guarantee that all eligible mates are male (since the first parent chosen is always female, as explained above). In other words, weights for females must be `0`. The `weights` vector given to the callback is guaranteed to satisfy this constraint. If sex is not enabled – in a hermaphroditic simulation, in other words – this constraint does not apply.

For example, a simple `mateChoice()` callback might look like this:

```
1000:2000 mateChoice(p2) {
    return weights ^ 2;
}
```

This defines a `mateChoice()` callback for generations `1000` to `2000` for subpopulation `p2`. The callback simply transforms the standard fitness-based probabilities by squaring them. Code like this could represent a situation in which fitness and mate choice proceed normally in one subpopulation (`p1`, here, presumably), but are altered by the effects of a social dominance hierarchy or male-male competition in another subpopulation (`p2`, here), such that the highest-fitness individuals tend to be chosen as mates more often than their (perhaps survival-based) fitness values would otherwise suggest. Note that by basing the returned weights on the `weights` vector supplied by SLiM, the requirement that females be given weights of `0` is finessed; in other situations, care would need to be taken to ensure that.

More than one `mateChoice()` callback may be defined to operate in the same generation. As with Eidos events, multiple callbacks will be called in the order in which they were defined. Furthermore, each callback will be given the `weights` vector returned by the previous callback – so the value of `weights` is not necessarily the default fitness-based weights, in fact, but is the result of all previous `weights()` callbacks for the current mate-choice event. In this way, the effects of multiple callbacks can "stack". If any `mateChoice()` callback returns `float(0)`, however –

indicating that no eligible mates exist, as described above – then the remainder of the callback chain will be short-circuited and a new first parent will immediately be chosen.

Note that matings in SLiM do not proceed in random order. Offspring are generated for each subpopulation in turn, and within each subpopulation the order of offspring generation is also non-random with respect to both the source subpopulation and the sex of the offspring. It is important, therefore, that `mateChoice()` callbacks are not in any way biased by the offspring generation order; they should not treat matings early in the process any differently than matings late in the process. Any failure to guarantee such invariance could lead to large biases in the simulation outcome. In particular, it is usually dangerous to activate or deactivate `mateChoice()` callbacks while offspring generation is in progress.

A wide variety of mate choice algorithms can easily be implemented with `mateChoice()` callbacks. For example, mating could be assortative, based upon some type of genetic similarity (section 11.1), or a sequential mate search could be conducted with some probability of failing to find a mate at all if the female is too choosy (section 11.2).

22.4 Defining child generation with a `modifyChild()` callback

Normally, a SLiM simulation defines child generation with its rules regarding selfing versus crossing, recombination, mutation, and so forth. However, one might wish to modify these rules in particular circumstances – by preventing particular children from being generated, by modifying the generated children in particular ways, or by generating children oneself. All of these dynamics can be handled in SLiM with the `modifyChild()` callback mechanism.

A `modifyChild()` callback is established in the input file with a syntax very similar to that of other callbacks:

```
[id] [gen1 [: gen2]] modifyChild([<subpop-id>]) { ... }
```

The `modifyChild()` callback may optionally be restricted to the children generated to occupy a specified subpopulation.

When a `modifyChild()` callback is called, a parent or parents have already been chosen, and a candidate child has already been generated. The genomes of the parent or parents are provided to the callback, as is the genome of the generated child. The callback may accept the generated child, modify it, substitute completely different genomic information for it, or reject it (causing a new parent or parents to be selected and a new child to be generated, which will again be passed to the callback).

In addition to the SLiM globals listed in section 22.1, a `modifyChild()` callback is supplied with additional information passed through global variables:

`child`	The generated child (an object of class `Individual`)
`childGenome1`	One genome of the generated child
`childGenome2`	The other genome of the generated child
`childIsFemale`	`T` if the child will be female, `F` if male (defined only if sex is enabled)
`parent1`	The first parent (an object of class `Individual`)
`parent1Genome1`	One genome of the first parent
`parent1Genome2`	The other genome of the first parent
`isCloning`	`T` if the child is the result of cloning
`isSelfing`	`T` if the child is the result of selfing (but see note below)
`parent2`	The second parent (an object of class `Individual`)
`parent2Genome1`	One genome of the second parent
`parent2Genome2`	The other genome of the second parent

`subpop`	The subpopulation in which the child will live
`sourceSubpop`	The subpopulation of the parents (`==subpop` if not a migration mating)

These globals may be used in the `modifyChild()` callback to decide upon a course of action. The `childGenome1` and `childGenome2` variables may be modified by the callback; whatever mutations they contain on exit will be used for the new child. Alternatively, they may be left unmodified (to accept the generated child as is). These variables may be thought of as the two gametes that will fuse to produce the fertilized egg that results in a new offspring; `childGenome1` is the gamete contributed by the first parent (the female, if sex is turned on), and `childGenome2` is the gamete contributed by the second parent (the male, if sex is turned on).

Importantly, a `logical` singleton return value is required from `modifyChild()` callbacks. Normally this should be `T`, indicating that generation of the child may proceed (with whatever modifications might have been made to the child's genomes). A return value of `F` indicates that generation of this child should not continue; this will cause new parent(s) to be drawn, a new child to be generated, and a new call to the `modifyChild()` callback. A `modifyChild()` callback that always returns `F` can cause SLiM to hang, so be careful that it is guaranteed that your callback has a nonzero probability of returning `T` for every state your simulation can reach.

Note that `isSelfing` is `T` only when a mating was explicitly set up to be a selfing event by SLiM; an individual may also mate with itself by chance (by drawing itself as a mate) even when SLiM did not explicitly set up a selfing event, which one might term *de facto* selfing. If you need to know whether a mating event was a *de facto* selfing event, you can compare the parents; self-fertilization will always entail `parent1==parent2`, even when `isSelfing` is `F`. See the recipe in section 12.4 for an example of how to use this to suppress *de facto* selfing. Since selfing is enabled only in non-sexual simulations, `isSelfing` will always be `F` in sexual simulations (and *de facto* selfing is also impossible in sexual simulations).

Note that matings in SLiM do not proceed in random order. Offspring are generated for each subpopulation in turn, and within each subpopulation the order of offspring generation is also non-random with respect to the source subpopulation, the sex of the offspring, and the reproductive mode (selfing, cloning, or autogamy). It is important, therefore, that `modifyChild()` callbacks are not in any way biased by the offspring generation order; they should not treat offspring generated early in the process any differently than offspring generated late in the process. Similar to `mateChoice()` callbacks, any failure to guarantee such invariance could lead to large biases in the simulation outcome. In particular, it is usually dangerous to activate or deactivate `modifyChild()` callbacks while offspring generation is in progress. When SLiM sees that `mateChoice()` or `modifyChild()` callbacks are defined, it randomizes the order of child generation within each subpopulation, so this issue is mitigated somewhat. However, offspring are still generated for each subpopulation in turn. Furthermore, in generations without active callbacks offspring generation order will not be randomized (making the order of parents nonrandom in the next generation), with possible side effects. In short, order-dependency issues are still possible and must be handled very carefully.

As with the other callback types, multiple `modifyChild()` callbacks may be registered and active. In this case, all registered and active callbacks will be called for each child generated, in the order that the callbacks were registered. If a `modifyChild()` callback returns `F`, however, indicating that the child should be generated, the remaining callbacks in the chain will not be called.

There are many different ways in which a `modifyChild()` callback could be used in a simulation; see the recipes in chapter 12 for illustrations of the power of this technique.

22.5 Defining recombination behavior with a `recombination()` callback

Typically, a simulation sets up a recombination map at the beginning of the run with `initializeRecombinationRate()`, and that map is used for the duration of the run. Less commonly, the recombination map is changed dynamically from generation to generation, with `Chromosome`'s method `setRecombinationRate()`; but still, a single recombination map applies for all individuals in a given generation. However, in unusual circumstances a simulation may need to modify the way that recombination works on an individual basis; for this, the `recombination()` callback mechanism is provided. This can be useful for models involving chromosomal inversions that prevent recombination within a region for some individuals (see section 13.5), for example, or for models of the evolution of recombination.

A `recombination()` callback is defined with a syntax much like that of other callbacks:

```
[id] [gen1 [: gen2]] recombination([<subpop-id>]) { ... }
```

The `recombination()` callback will be called during the generation of every gamete during the generation(s) in which it is active. It may optionally be restricted to apply only to gametes generated by parents in a specified subpopulation, using the `<subpop-id>` specifier.

When a `recombination()` callback is called, a parent has already been chosen to generate a gamete, and candidate recombination breakpoints for use in recombining the parental genomes have been drawn. The genomes of the focal parent are provided to the callback, as is the focal parent itself (as an `Individual` object) and the subpopulation in which it resides. Furthermore, the proposed breakpoints are provided to the callback, divided into three categories: ordinary recombination breakpoints, and start/end positions for gene conversion events (if gene conversion is enabled). The callback may modify these variables in order to change the breakpoints used, in which case it must return `T` to indicate that changes were made, or it may leave the proposed breakpoints unmodified, in which case it must return `F`. (The behavior of SLiM is undefined if the callback returns the wrong `logical` value.)

In addition to the SLiM globals listed in section 22.1, then, a `recombination()` callback is supplied with additional information passed through global variables:

`individual`	The focal parent that is generating a gamete
`genome1`	One genome of the focal parent; this is the initial copy strand
`genome2`	The other genome of the focal parent
`subpop`	The subpopulation to which the focal parent belongs
`breakpoints`	An `integer` vector of ordinary recombination breakpoints
`gcStarts`	An `integer` vector of the start positions of gene conversion spans
`gcEnds`	An `integer` vector of the end positions of gene conversion spans

These globals may be used in the `recombination()` callback to determine the final recombination breakpoints used by SLiM. The positions in `gcStarts` and `gcEnds` constitute matched pairs (a corresponding end for each start), so the lengths of those two vectors are guaranteed to be equal. If values are set into `breakpoints`, `gcStarts`, and/or `gcEnds`, the new values must be of type `integer`, and `gcStarts` and `gcEnds` must be set to vectors of the same length (again, constituting matched pairs). If any of `breakpoints`, `gcStarts`, or `gcEnds` are modified by the callback, `T` should be returned, otherwise `F` should be returned (this is a speed optimization, so that SLiM does not have to spend time checking for changes when no changes have been made).

The positions specified in `breakpoints`, `gcStarts`, and `gcEnds` mean that a crossover will occur immediately *before* the specified base position (between the preceding base and the specified base, in other words). The genome specified by `genome1` will be used as the initial copy strand when SLiM executes the recombination; this cannot presently be changed by the callback.

In this design, the recombination callback does not specify a custom recombination map (although that is a possible extension to this design that could be implemented if it would be useful). Instead, the callback can add or remove breakpoints at specific locations. To implement a chromosomal inversion, as is done in the recipe in section 13.5, for example, if the parent is heterozygous for the inversion mutation then crossovers within the inversion region are removed by the callback. As another example, to implement a model of the evolution of the overall recombination rate, a model could (1) set the global recombination rate to the highest rate attainable in the simulation, (2) for each individual, within the `recombination()` callback, calculate the fraction of that maximum rate that the focal individual would experience based upon its genetics, and (3) probabilistically remove proposed crossover points based upon random uniform draws compared to that threshold fraction, thus achieving the individual effective recombination rate desired. Other similar treatments could actually vary the effective recombination map, not just the overall rate, by removing proposed crossovers with probabilities that depend upon their position, allowing for the evolution of localized recombination hot-spots and cold-spots. Crossovers and gene conversion events may also be added, not just removed, by `recombination()` callbacks.

Note that the positions in `breakpoints`, `gcStarts`, and `gcEnds` are not, in the general case, guaranteed to be sorted or uniqued; in other words, positions may appear out of order, and the same position may appear more than once. After all `recombination()` callbacks have completed, the positions from `breakpoints`, `gcStarts`, and `gcEnds` will be merged together into a single vector, sorted, uniqued, and used as the crossover points in generating the prospective gamete genome. The essential point here is that if the same position occurs more than once, across `breakpoints`, `gcStarts`, and `gcEnds`, the multiple occurrences of the position do not cancel; SLiM does not cross over and then "cross back over" given a pair of identical positions. Instead, the multiple occurrences of the position will simply be uniqued down to a single occurrence.

As with the other callback types, multiple `recombination()` callbacks may be registered and active. In this case, all registered and active callbacks will be called for each gamete generated, in the order that the callbacks were registered.

22.6 Defining interaction behavior with an `interaction()` callback

The `InteractionType` class (section 21.7) provides various built-in interaction functions that translate from distances to interaction strengths. However, it may sometimes be useful to define a custom function for that purpose; for that reason, SLiM allows `interaction()` callbacks to be defined that modify the standard interaction strength calculated by `InteractionType`. In particular, this mechanism allows the strength of interactions to depend upon not only the distance between individuals, but also the genetics and other state of the individuals, the spatial position of the individuals, and other environmental variables.

An `interaction()` callback is called by SLiM when it is determining the strength of the interaction between one individual (the receiver of the interaction) and another individual (the exerter of the interaction). This may occur when the `evaluate()` method of `InteractionType` is called, if immediate evaluation is requested (see section 21.7.2); or it may occur at some point after evaluation of the `InteractionType`, when the interaction strength is needed, if immediate evaluation was not requested. This means that `interaction()` callbacks() may be called at a variety of points in the generation cycle, unlike the other callback types in SLiM, which are each called at a specific point. If you write an `interaction()` callback, you need to take this into account; assuming that the generation cycle is at a particular stage, or even that the generation count is the same as it was when `evaluate()` was called, may be dangerous.

When an interaction strength is needed, the first thing SLiM does is calculate the default interaction strength using the interaction function that has been defined for the InteractionType (see section 21.7). If the receiver is the same as the exerter, the interaction strength is always zero; and in spatial simulations if the distance between the receiver and the exerter is greater than the maximum distance set for the InteractionType, the interaction strength is also always zero. In these cases, interaction() callbacks will not be called, and there is no way to redefine these interaction strengths.

Otherwise, SLiM will then call `interaction()` callbacks that apply to the interaction type and subpopulation for the interaction being evaluated. An `interaction()` callback is defined with a variation of the syntax used for other callbacks:

```
[id] [gen1 [: gen2]] interaction(<int-type-id> [, <subpop-id>]) { ... }
```

For example, if the callback were defined as:

```
1000:2000 interaction(i2, p3) { 1.0; }
```

then an interaction strength of `1.0` would be used for all interactions of interaction type `i2` in subpopulation `p3` from generation `1000` to generation `2000`.

In addition to the SLiM globals listed in section 22.1, an `interaction()` callback is supplied with some additional information passed through global variables:

`distance`	The distance from receiver to exerter, in spatial simulations; `NAN` otherwise
`strength`	The default interaction strength calculated by the interaction function
`receiver`	The individual receiving the interaction (an object of class `Individual`)
`exerter`	The individual exerting the interaction (an object of class `Individual`)
`subpop`	The subpopulation in which the receiver and exerter live

These globals may be used in the `interaction()` callback to compute an interaction strength. To simply use the default interaction strength that SLiM would use if a callback had not been defined for interaction type `i1`, for example, you could do this:

```
interaction(i1) {
    return strength;
}
```

Usually an `interaction()` callback will modify that default strength based upon factors such as the genetics of the receiver and/or the exerter, the spatial positions of the two individuals, or some other simulation state. Any finite `float` value greater than or equal to `0.0` may be returned. The value returned will be cached by SLiM; if the interaction strength between the same two individuals is needed again later, the `interaction()` callback will not be called again (something to keep in mind if the interaction strength includes a stochastic component).

More than one `interaction()` callback may be defined to operate in the same generation. As with other callbacks, multiple callbacks will be called in the order in which they were defined in the input file. Furthermore, each callback will be given the `strength` value returned by the previous callback – so the value of `strength` is not necessarily the default value, in fact, but is the result of all previous `interaction()` callbacks for the interaction in question. In this way, the effects of multiple callbacks can "stack".

The `interaction()` callback mechanism is extremely powerful and flexible, allowing any sort of user-defined interactions whatsoever to be queried dynamically using the methods of `InteractionType`. However, in the general case a simulation may call for the evaluation of the interaction strength between each individual and every other individual, making the computation of the full interaction network an O(N^2) problem. Since `interaction()` callbacks may be called for each of those N^2 interaction evaluations, they can slow down a simulation considerably, so it is recommended that they be used sparingly. This is the reason that the various interaction functions of `InteractionType` were provided; when an interaction does not depend upon individual state, the intention is to avoid the necessity of an `interaction()` callback altogether. Furthermore, constraining the number of cases in which interaction strengths need to be calculated – using a short maximum interaction distance, querying the nearest neighbors of the focal individual rather than querying all possible interactions with that individual, and specifying the reciprocality and sex segregation of the `InteractionType`, for example – may greatly decrease the computational overhead of interaction evaluation.

22.7 Defining reproduction behavior with a `reproduction()` callback

In WF models (the default model type in SLiM), the SLiM core manages the reproduction of individuals in each generation. In nonWF models, however, reproduction is managed by the model script, in `reproduction()` callbacks. These callbacks may only be defined in nonWF models.

A `reproduction()` callback is defined with a syntax much like that of other callbacks:

```
[id] [gen1 [: gen2]] reproduction([<subpop-id> [, <sex>]]) { ... }
```

The `reproduction()` callback will be called once for each individual during the generation(s) in which it is active. It may optionally be restricted to apply only to individuals in a specified subpopulation, using the `<subpop-id>` specifier; this may be a subpopulation specifier such as `p1`, or `NULL` indicating no restriction. It may also optionally be restricted to apply only to individuals of a specified sex (in sexual models), using the `<sex>` specifier; this may be `"M"` or `"F"`, or `NULL` indicating no restriction.

When a `reproduction()` callback is called, the expectation is that the callback will trigger the reproduction of a focal individual by making method calls to add new offspring individuals. Typically the offspring added are the offspring of the focal individual, and typically they are added to the subpopulation to which the focal individual belongs, but neither of these is required; a `reproduction()` callback may add offspring generated by any parent(s), to any subpopulation. The focal individual is provided to the callback (as an `Individual` object), as are its genomes and the subpopulation in which it resides.

In addition to the SLiM globals listed in section 22.1, then, a `reproduction()` callback is supplied with additional information passed through global variables:

`individual`	The focal individual that is expected to reproduce
`genome1`	One genome of the focal individual
`genome2`	The other genome of the focal individual
`subpop`	The subpopulation to which the focal individual belongs

At present, the return value from `reproduction()` callbacks is not used, and must be `void` (i.e., a value may not be returned). It is possible that other return values will be defined in future.

It is possible, of course, to do actions unrelated to reproduction inside `reproduction()` callbacks, but it is not recommended. The `late()` event phase of the previous generation provides an opportunity for actions immediately before reproduction, and the `early()` event phase of the current generation provides an opportunity for actions immediately after reproduction, so only actions that are intertwined with reproduction itself should occur in `reproduction()` callbacks. Besides providing conceptual clarity, following this design principle will also decrease the probability of bugs, since actions that are unrelated to reproduction should not influence or be influenced by the dynamics of reproduction.

As with the other callback types, multiple `reproduction()` callbacks may be registered and active. In this case, all registered and active callbacks will be called for each individual, in the order that the callbacks were registered.

22.8 Further details on Eidos events and callbacks

Section 22.1 described Eidos events, and sections 22.2 – 22.6 described several different Eidos callbacks that can be defined to modify the standard behavior of SLiM. This section describes a few additional details that apply to events and callbacks. These details were mentioned previously, but were not detailed, in the interests of simplicity; they are of interest mainly to the most advanced users of SLiM.

Every Eidos block – an event or a callback – is defined in SLiM using a class called `SLiMEidosBlock`. All of the registered instances of this class – all of the Eidos blocks scheduled to run in the simulation – are available through the `scriptBlocks` property of `SLiMSim` (section 21.12.2). New script blocks may be added programmatically (rather than in the SLiM input file) using `SLiMSim`'s `-register...()` methods; those methods take a `string` parameter, which is interpreted as Eidos code. Existing script blocks may be deregistered, which removes them from the current simulation permanently, using the `-deregisterScriptBlock()` method of `SLiMSim`. In this way, the script blocks defined in the SLiM input file are only the beginning; by adding and removing script blocks dynamically, SLiM simulations can modify their own code as they run. Obviously this feature would, if used indiscriminately, result in incomprehensible and unmaintainable code; but in some circumstances, it can be extremely useful and powerful.

Generally, code that manipulates `SLiMEidosBlock` objects finds the operand blocks using the `id` property of `SLiMEidosBlock`. Alternatively, a script block that references itself (to deregister itself, for example, or to set its own `active` property) can use a global constant called `self` that is defined whenever an Eidos block is executing. The `self` constant refers to the executing `SLiMEidosBlock` object. It may be passed to `-deregisterScriptBlock()` in order to deregister the current block; this is safe to do, as the executing block will not actually be deregistered until it has finished executing. It may also be used to change the properties of the currently executing script block.

In particular, `SLiMEidosBlock` defines an `integer` property, `active`. The `active` property is normally `-1`; this means that script blocks are normally active. If set to `0`, the script block will be inactive for the remainder of the current generation; it will not be called or used in any way (except that if it is currently executing when `active` is set to `0`, that execution will complete). At the beginning of each generation, prior to the execution of any script blocks, the `active` flag of all registered script blocks will be set back to `-1`, activating them all again; if you want a script block to be inactive permanently, you must deregister it rather than just marking it as inactive. Values other than `-1` may be used for `active`; any value other than `0` indicates that the block is active (because `active` is evaluated as a `logical` value; only `0` is `F`). This facility is provided to allow script blocks to run a limited number of times in each generation; the block can check whether `active` is `-1` (indicating that it is being called for the first time in a generation), and can set `active` to a counter value. In each call to the script block, the script can decrement the `active` counter by `1`; when it reaches `0`, the block will not be called again in that generation. The `active` property could even be used to implement a more complex state machine.

The precise way in which SLiM handles the scheduling of `SLiMEidosBlock` objects may be important for some scripts. Because new script blocks can be added dynamically with `-register...()`, and existing blocks can be removed with `-deregisterScriptBlock()`, the right way to schedule block is not entirely clear. If SLiM is partway through generating children, and then a new `modifyChild()` callback is added, for example, should that callback be used for the remaining children generated in the current generation? What if an existing `modifyChild()` callback is removed, partway through the process of child generation – should that callback stop being used immediately? For consistency, SLiM's answer to both of these questions is "no"; a consistent set of scripts are used across each stage of each generation. However, if a `modifyChild()` callback is added before generating children begins, then that callback is used in the same generation. In essence, the rule is this: whenever SLiM starts on a new stage of the generational life cycle that involves calling a particular kind of Eidos block, SLiM gathers up a list of all of the currently defined script blocks applicable to that stage, and it uses that list throughout the duration of that stage, regardless of what changes are made to the registered script blocks during the stage. The state of the `active` property of each script block is checked immediately before each time that the script block is called, however; the `active` property is specifically intended to change the active status of a script block within a single generation.

23. SLiM output formats

In addition to allowing custom output in any format whatsoever, produced with Eidos code, SLiM also has numerous ways to produce output in fixed formats using built-in methods:

- Methods on `SLiMSim` (section 21.12.2): `outputFull()`, `outputFixedMutations()`, and `outputMutations()`.
- Methods on `Subpopulation` (section 21.13.2): `outputSample()`, `outputMSSample()`, and `outputVCFSample()`.
- Methods on `Genome` (section 21.3.2): `output()`, `outputMS()`, and `outputVCF()`.

The documentation cited for these classes above summarizes the method calls themselves, but does not document the precise format they produce; that will be covered in this chapter.

Note that these methods, and the format of the output produced by SLiM, changed in various ways in SLiM version 2.1. This documentation will discuss only the format of output from SLiM 2.1 and later, for simplicity.

As will be shown below, all of these output methods can generate a header line beginning with the tag `#OUT:` followed by (1) the generation in which the output was generated, (2) a one- or two-letter output type code, (3) additional values depending upon the output type, and (4) if output was directed to a file, the filename to which output was directed (except in the case of the `SLiMSim` method `outputMutations()`). The output code in the header line may be used to detect which type of output follows, which is useful for automated parsing of simulation output files. The codes are as follows:

`SLiMSim` methods:	
`outputFull()`	`A`
`outputFixedMutations()`	`F`
`outputMutations()`	`T`
`Subpopulation` methods:	
`outputSample()`	`SS`
`outputMSSample()`	`SM`
`outputVCFSample()`	`SV`
`Genome` methods:	
`output()`	`GS`
`outputMS()`	`GM`
`outputVCF()`	`GV`

All of these methods support output to either the SLiM output stream or to a designated file. When output is sent to a file, all of these methods support either overwriting an existing file at the specified path, or appending to any existing file.

These output methods are some of the more complex methods in SLiM, often with many optional arguments that are typically specified by name. See the Eidos manual for discussion of how to use optional arguments and named arguments, how to interpret complex type-specifiers and method signatures, and so forth; that information is not repeated here.

23.1 `SLiMSim` output methods

The output methods of `SLiMSim` produce output regarding state that spans the whole population, rather than just a single subpopulation or a selected set of genomes.

23.1.1 `outputFull()`

The `outputFull()` method outputs complete information on all subpopulations, individuals, and genomes, including all currently segregating mutations (but not including mutations that have fixed and been converted into `Substitution` objects). Sample output for `outputFull()`, abbreviated with ellipses:

```
#OUT: 10000 A
Version: 3
Populations:
p1 50 H
p2 50 H
...
Mutations:
10 387752 m1 1308 0 0.5 p2 9404 130
47 387966 m1 5994 0 0.5 p1 9415 130
...
Individuals:
p1:i0 H p1:0 p1:1
p1:i1 H p1:2 p1:3
...
Genomes:
p1:0 A 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19...
p1:1 A 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84...
...
```

The header line begins with `#OUT:` and then gives the generation in which the output was produced, followed by an `A` (for "all"). If the output is sent to a file with `outputFull()`'s `filePath` option, this is followed by the full path of the file to which the output was saved; for example:

```
#OUT: 10000 A /Users/bhaller/Desktop/full.txt
```

Beginning in SLiM 2.3, the header line followed by a single line that indicates the version of the `outputFull()` file format. SLiM 2.3's format is indicated by a version number of `3` (for internal reasons); if the version line is missing, it may be inferred that the file format is pre-2.3. The reason for this addition is that it allows SLiM (and other software) to more accurately read in output files generated by different versions of SLiM, since the version number indicates what the reader software can expect to find in the file. A version of `4` is used by SLiM 3.0 and later to indicate that age values are included in the Individuals section; see below.

After this comes the Populations section, which lists all currently existing subpopulations. First is given the subpopulation's identifier, such as `p1`. Next is listed its current size, in individuals (not genomes). Finally, an `H` indicates that the population is composed of hermaphroditic individuals; if sex has been enabled with `initializeSex()`, this will instead be an `S` followed by the current sex ratio of the subpopulation (i.e., `S 0.5`).

Next is the Mutations section, which lists all of the currently segregating mutations in the population. Each mutation is listed on a separate line. The first field is a within-file numeric identifier for the mutation, beginning at `0` and counting up (although mutations are not listed in sorted order according to this value); see below for a note on why this field exists. Second is the mutation's `id` property (see section 21.8.1), a within-run unique identifier for mutations that does not change over time, and can thus be used to match up information on the same mutation within multiple output dumps made at different times. Third is the identifier of the mutation's mutation type, such as `m1`. Fourth is the position of the mutation on the chromosome, as a zero-based base position. Fifth is the selection coefficient of the mutation, and sixth is its dominance coefficient (the latter being a property of the mutation type, in fact). Seventh is the identifier for the subpopulation in which the mutation originated, and eighth is the generation in which it originated. Finally, the ninth field gives the mutation's prevalence: an integer count of the number of times that it occurs in any genome in the population.

Following this section is the Individuals section. This describes each individual in each subpopulation and specifies which genomes belong to it. The first field is an identifier for the individual, such as `p1:i0` (which indicates the `0`th individual in `p1`). Next is the sex of the individual: `H` for a hermaphrodite, or if sex has been enabled, `M` for a male or `F` for a female. Following that come two genome specifiers, of the form `p1:0` (indicating the `0`th genome in `p1`).

Beginning in SLiM 2.3, the genome specifiers may be followed by spatial positioning information for each individual. This will be the case if continuous space has been enabled with the `dimensionality` parameter to `initializeSLiMOptions()` and the `spatialPositions` parameter to `outputFull()` is `T` (which is the default). If both of those preconditions are satisfied, then the properties of `Individual` that represent spatial positions (`x`, `y`, and/or `z`) will be output as floating-point values. Only properties that are included in the dimensionality of the simulation will be output. For example, if the simulation has been configured to have dimensionality `"xy"` with `initializeSLiMOptions()`, then the Individuals section might look like this:

```
Individuals:
p1:i0 H p1:0 p1:1 0.397687 0.522408
p1:i1 H p1:2 p1:3 0.066159 0.74749
...
```

The first floating-point value on each line is the value of `x` for that individual; the second is the value of `y`. The value of the `z` property is not output because the *z*-coordinate is not included in the dimensionality of the simulation. If `spatialPositions=F` were specified in the call to `outputFull()`, this positional information would not be output and the file format would be identical to that produced by version 2.1 (apart from the addition of the Version line in SLiM 2.3, described above).

Beginning in SLiM 3.0, the genome specifiers may be followed by the age of each individual. This will be the case if the simulation is using the nonWF model type (which is *not* the default) and the `ages` parameter to `outputFull()` is `T` (which is the default). If both of those preconditions are satisfied, then the `age` property of each individual will be output as an integer at the end of each line in the Individuals section, following the genome specifiers and (if present) the optional spatial positioning information controlled by `spatialPositions`. If age information is not output, the output format is just as it was before SLiM 3.0, for backward compatibility. Note that if age information is included in the output, the version number specified in the Version line will be `4`; if not, the version will remain `3` (as it was before SLiM 3.0).

Last comes the Genomes section, which specifies all of the mutations carried by each genome in the population. The first field is a genome specifier, such as `p1:0`, as described above. Second is the type of genome: an `A` for an autosome, or an `X` or `Y` for those types if modeling of sex chromosomes has been enabled. This is followed by a list of within-file mutation identifiers, as given in the Mutations section described above, that identify all the mutations carried on the genome. Alternatively, if the genome is a "null genome" that is not allowed to carry any mutations in SLiM (such as a `Y` chromosome if SLiM is modeling the `X`), the tag `<null>` will appear instead of any mutation identifiers.

The reader might wonder why the within-file index for mutations (the first field in each mutation's output line) even exists. Couldn't the mutation's `id` (the second field) be used for that purpose, since it also uniquely identifies mutations? The answer is: yes, in principle it could. In practice, however, `id` values for mutations are often very large numbers – six, seven, or even more digits long. Because the bulk of a SLiM output file consists of the sequences of mutation identifiers listed in the Genome section, using small zero-based numbers for these identifiers actually makes SLiM's output files markedly smaller than they would be if mutation `id` values were used instead. Keeping output files small is an end in itself, since disk space is limited, but also has the benefit of making file writes and reads faster.

On the topic of file size and read/write speed, note that the `outputFull()` method also provides the option of writing out a binary file. The format of that file is not documented, and is subject to change at any time (although we will try to preserve backward compatibility when possible). Binary files can be smaller, and their read and write times are much faster.

Note that the output from `outputFull()` is the only output format that SLiM can read as well as write. This is done with the `readFromPopulationFile()` method of `SLiMSim` (see section 21.12.2).

23.1.2 `outputFixedMutations()`

The `outputFixedMutations()` method outputs information on all mutations that have fixed and been turned into Substitution objects. It therefore complements the information produced by `outputFull()`. Sample output for `outputFixedMutations()`, abbreviated with ellipses:

```
#OUT: 10000 F
Mutations:
0 390 m1 701 0 0.5 p2 20 650
1 1114 m1 957 0 0.5 p1 55 650
...
```

The header line has the standard SLiM output tag `#OUT:` followed by the generation and then an `F` (for "fixed"). If the output is sent to a file with `outputFixedMutations()`'s `filePath` option, this is followed by the full path of the file to which the output was saved.

Following this is one section of output, Mutations. This lists every mutation that has fixed and been turned into a Substitution object. The first eight fields used are identical to those used in the Mutations section of `outputFull()` as described above: (1) a within-file identifier counting upward from 0, (2) the mutation's `id` property that uniquely identifies in within a run, (3) the identifier for the mutation type, (4) the position on the chromosome, (5) the selection coefficient, (6) the dominance coefficient, (7) the originating subpopulation, and (8) the origination generation. The last field is different, however; instead of being a prevalence (which would be useless since these mutations are, by definition, fixed), this field indicates the generation in which the mutation was converted to a `Substitution` object (which is the same as the generation in which it fixed, unless you are dynamically changing the `convertToSubstitution` flag).

23.1.3 `outputMutations()`

The `outputMutations()` method is intended to be used to output information about particular mutations of interest that are being "tracked" – mutations of a particular mutation type, for example, or perhaps a specific introduced mutation. Sample output for `outputMutations()`:

```
#OUT: 10000 T p1 388376 m1 673 0 0.5 p2 9434 43
#OUT: 10000 T p2 388376 m1 673 0 0.5 p2 9434 27
```

These two lines of output are the result of an `outputMutations()` call requesting output for just a single mutation. The first line gives information about the prevalence of the mutation in subpopulation `p1`, whereas the second line gives the same for `p2`. If you requested output for more than one mutations, you get a line for each mutation requested:

```
#OUT: 10000 T p1 388376 m1 673 0 0.5 p2 9434 43
#OUT: 10000 T p1 388788 m1 9394 0 0.5 p2 9455 57
#OUT: 10000 T p1 390206 m1 6232 0 0.5 p2 9523 57
...
```

```
#OUT: 10000 T p2 388376 m1 673 0 0.5 p2 9434 27
#OUT: 10000 T p2 388788 m1 9394 0 0.5 p2 9455 73
#OUT: 10000 T p2 390206 m1 6232 0 0.5 p2 9523 73
...
```

Note that the output is sorted by subpopulation, not by mutation, so the lines for a particular mutation do not necessarily end up adjacent. If a mutation is not present in a given subpopulation at all, no output line is produced for that mutation in that subpopulation.

The format of each output line follows a similar pattern to other output methods. First comes the `#OUT:` tag, followed by the generation and then a `T` (for "tracked", for historical reasons). Next comes the subpopulation identifier, such as `p1`, for which the line is being produced. The remaining fields are the same mutation information as produced by `outputFull()`: (1) the mutation's `id` property, (2) the identifier of its mutation type, (3) its position, (4) its selection coefficient, (5) its dominance coefficient, (6) origin subpopulation identifier, (7) origin generation, and (8) prevalence. Note that even if `outputMutations()`'s `filePath` parameter is used to send the output to a file, the filename is not added at the end of the header line as it is with SLiM's other output commands, to keep the output from this command concise (since it really consists of nothing but header lines).

23.2 Subpopulation output methods

The output methods of `Subpopulation` produce output about the mutations carried by a sampled subset of the `Subpopulation`. Three different formats of output are presently available: SLiM's native format, MS, and VCF.

23.2.1 `outputSample()`

The `outputSample()` method takes a random sample of genomes from the subpopulation as requested (with options regarding sample size, replacement, and sex) and outputs information on them in SLiM's native format. If the sampling options provided by `outputSample()` are insufficiently flexible, the `output()` method of `Genome` is a more general-purpose method (see section 23.3.1). Sample output for `outputSample()`, abbreviated with ellipses:

```
#OUT: 10000 SS p1 10
Mutations:
65 587710 m1 1308 0 0.5 p2 9404 5
101 587924 m1 5994 0 0.5 p1 9415 5
...
Genomes:
p1:0 A 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23...
p1:1 A 0 1 2 3 4 5 6 8 9 10 49 50 11 12 13 14 15 16 17 18 51 19 22 23...
...
```

The header line starts with the usual tag, `#OUT:`, followed by the generation and then `SS` (representing "sample, SLiM format"). It then gives the identifier for the subpopulation sampled, such as `p1`, and finally the size of the sample (in genomes, not individuals). If the output is sent to a file with `outputSample()`'s `filePath` option, this is followed by the full path of the file to which the output was saved.

This is followed by a Mutations section and then a Genomes section. The formats of these is identical to the same sections in the output of `outputFull()`, described in section 23.1.1, except that the prevalence values given for mutations are their prevalence within the sample of genomes, not in the population as a whole. Note that the Individuals section provided by `outputFull()` is also not present in the output from `outputSample()`, because the sample is of genomes, not complete individuals.

23.2.2 `outputMSSample()`

The `outputMSSample()` method takes a random sample of genomes from the subpopulation as requested (with options regarding sample size, replacement, and sex) and outputs information on them in MS format. If the sampling options provided by `outputMSSample()` are insufficiently flexible, the `outputMS()` method of `Genome` is a more general-purpose method (see section 23.3.2). Sample output for `outputMSSample()`, abbreviated with ellipses:

```
#OUT: 10000 SM p1 10
//
segsites: 179
positions: 0.1308131 0.4991499 0.5994599 0.6999700 0.9599960...
00101001000001101011111000000011111000100100111100001000011000100000...
00101001000001101011111000000011111000100100111100001000011000100000...
...
```

The first line is a header in the same format as for `outputSample()`, as described in the previous section. The output type code here, `SM`, represents "sample, MS format". The `outputMSSample()` method allows output to be sent to a file, with the optional `filePath` argument. In this case, the `#OUT:` header line is not emitted, since it would not be conformant with the MS data format specification.

This is followed by an empty comment line `//`, and then a line stating the total number of segregating sites output. Note that, as with all other output methods in SLiM, these sites are segregating *in the population*, but every genome in the sample may be identical at a given site.

Next comes a line giving the position on the chromosome of each of the segregating sites. These positions have been converted by SLiM from base positions to floating-point positions in the interval [0,1] as expected for the MS format. Note that SLiM allows multiple mutations at exactly the same position, so even without roundoff (which may also be an issue for very long chromosomes), two positions in this list may be specified with exactly the same number.

Finally, the output has one line for each genome in the sample. Each line is a simple sequences of `0`'s and `1`'s, indicating whether the genome in question possesses (`1`) or does not possess (`0`) the mutation at the corresponding position in the list of positions.

23.2.3 `outputVCFSample()`

The `outputVCFSample()` method takes a random sample of individuals (*not* genomes!) from the subpopulation as requested (with options regarding sample size, replacement, and sex) and outputs information on them. If the sampling options provided by `outputVCFSample()` are insufficiently flexible, the `outputVCF()` method of `Genome` is a more general-purpose method (see section 23.3.3). Sample output for `outputVCFSample()`, abbreviated with ellipses:

```
#OUT: 10000 SV p1 10
##fileformat=VCFv4.2
##fileDate=20160613
##source=SLiM
##INFO=<ID=MID,Number=1,Type=Integer,Description="Mutation ID in SLiM">
##INFO=<ID=S,Number=1,Type=Float,Description="Selection Coefficient">
##INFO=<ID=DOM,Number=1,Type=Float,Description="Dominance">
##INFO=<ID=PO,Number=1,Type=Integer,Description="Population of Origin">
##INFO=<ID=GO,Number=1,Type=Integer,Description="Generation of Origin">
##INFO=<ID=MT,Number=1,Type=Integer,Description="Mutation Type">
##INFO=<ID=AC,Number=1,Type=Integer,Description="Allele Count">
##INFO=<ID=DP,Number=1,Type=Integer,Description="Total Depth">
##INFO=<ID=MULTIALLELIC,Number=0,Type=Flag,Description="Multiallelic">
##FORMAT=<ID=GT,Number=1,Type=String,Description="Genotype">
```

```
#CHROM POS ID REF ALT QUAL FILTER INFO FORMAT i0 i1 i2 i3 i4 i5...
1 1309 . A T 1000 PASS
MID=987550;S=0;DOM=0.5;PO=2;GO=9404;MT=1;AC=11;DP=1000 GT 0|1 0|0 0|1...
1 5995 . A T 1000 PASS
MID=987764;S=0;DOM=0.5;PO=1;GO=9415;MT=1;AC=11;DP=1000 GT 0|1 0|0 0|1...
...
```

The first line is a header, similar to that produced by `outputSample()` and `outputMSSample()`. The output code `SV` here represents "sample, VCF format". The `outputVCFSample()` method allows output to be sent to a file, with the optional `filePath` argument. In this case, the `#OUT:` header line is not emitted, since it would not be conformant with the VCF data format specification.

Following that is the VCF header, which provides various information about the information in the file; the VCF format is quite complex so we will not attempt to document it in detail here. Note that the `INFO` fields provided by SLiM include fields for a lot of SLiM-specific information that is not part of the VCF standard itself: the mutation's `id` property, selection and dominance coefficients, subpopulation of origin and generation of origin, and mutation type (the numeric part of a mutation type identifier like `m1`). These will have no meaning to most VCF tools, but may be useful for filtering or other analysis. The VCF header also describes two standard `INFO` tags: `AC` and `DP`. `AC` gives the "allele count", the number of occurrences of the given mutation within the sample. `DP` gives the "total depth", a property of empirical genomic samples that is meaningless for SLiM output; it is supplied, and is always equal to `1000`, in SLiM output to facilitate processing with VCF tools that expect this tag to be present. The last `INFO` tag described in the header is `MULTIALLELIC`; it is discussed below.

Following the VCF header are lines describing each mutation. Because of word-wrapping and line-breaking issues, these lines look a little funny here, but this is actually a single line, with fields separated by tab characters:

```
1 1309 . A T 1000 PASS
MID=987550;S=0;DOM=0.5;PO=2;GO=9404;MT=1;AC=11;DP=1000 GT 0|1 0|0 0|1...
```

These fields correspond to the column headings given in the last line of the VCF header:

```
#CHROM POS ID REF ALT QUAL FILTER INFO FORMAT i0 i1 i2 i3 i4 i5...
```

The first field is the chromosome identifier; SLiM always emits `1` for this. Next is the position of the mutation; note that VCF uses `1`-based positions, so this is the position used internally by SLiM plus `1`. The next five fields have VCF-oriented meanings that are unimportant for SLiM; they will always be `. A T 1000 PASS`. The next field is very long, and consists of a series of INFO tags separated by semicolons; the meaning of those fields is as specified by the `##INFO` lines in the VCF header. Next comes a `GT` tag indicating the start of genotype data, and finally a sequence of "calls" of the format `0|0`, `0|1`, `1|0`, or `1|1`, indicating whether a given individual in the sample possessed (`1`) or did not possess (`0`) the mutation in each of its two genomes. This data has essentially the same meaning as MS-format data, but in a notation that groups the 0's and 1's into homologous chromosomes in diploid individuals.

There are several things to note about this. First of all, calls are normally diploid (`0|0`, `1|0`, etc.), but if SLiM is modeling sex chromosomes, calls may be haploid instead (just a `0` or a `1`). For example, if you are modeling the X chromosome, males will be emitted as haploid while females will be emitted as diploid. There is no way to represent a `0`-ploid individual in VCF format, so if you are modeling the `Y` chromosome you may not include females in your sample; there would be no genetic information to emit for them.

Second, it is important to emphasize that VCF output, unlike all other output from SLiM, is based on individuals, not on genomes. The subpopulation sample taken by `outputVCFSample()` is a sample of individuals, not genomes, and thus a sample of size 10 will include twice as many genomes as a sample of size 10 would include for `outputMSSample()` or `outputSample()`.

Third, you might have noticed one incongruous `INFO` field in the VCF header above, called `MULTIALLELIC`. This is used by SLiM to designate mutations that occur at chromosome positions that have other segregating mutations also at the same position; such mutations will be tagged `MULTIALLELIC` in their `INFO` field information. In essence, the problem is this. SLiM is, in a sense, an infinite-alleles-per-site model. Any number of mutations can occur at the same position, all having different selection and dominance coefficients, etc., and these mutations can even co-occur within a single genome. VCF format, on the other hand, is more tightly tied to the biological reality of genetic information, that a given position has only four possible bases (A, T, G, C) ignoring epigenetic information like methylation. There is no very graceful way to wedge SLiM's perspective into VCF format, so we simply emit each mutation as its own VCF line. However, many VCF analysis tools may choke on this, or produce incorrect results, because VCF files normally contain only a single line per base position. In order to help alleviate this issue, SLiM tags all lines that possess this problem with the `MULTIALLELIC` tag. You can use this tag to filter out those sites – either to treat them specially, or to simply exclude them from your analysis. If you want to exclude them completely, you can also request that with a flag value passed to `outputVCFSample()`, in which case all lines that would have been tagged `MULTIALLELIC` will be suppressed.

Finally, note that SLiM designates all mutations as being a change from an A to a T. Since SLiM has no concept of nucleotide sequence, this is simply an arbitrary choice. If you wished to construct a FASTA file for the ancestral sequence, for example, it would simply be the length of the chromosome, filled with A's.

23.3 Genome output methods

The output methods of `Genome` produce output about the specific vector of `Genome` objects for which the method is called. Whereas the sampling output methods of `Subpopulation` limit you to a sample drawn from a single subpopulation, and provide only a few options regarding how that sample is conducted, with the `Genome` output methods you can construct your own vector of genomes in whatever way you wish, and produce standardized output from that sample. The `sample()` function of Eidos may prove useful for this, providing options such as weighted sampling that Subpopulation's methods don't support. The `Individual` class of SLiM may also be useful; you can get a vector of individuals from the subpopulations you are interested in, use `sample()` to get a sample of individuals from that vector, get the genomes from those individuals using the `genomes` property of `Individual`, and then produce output from the resulting vector of genomes using these methods.

Incidentally, you might wonder why these Genome output methods behave differently from most Eidos methods – they do not multicast out to all of the objects in the target vector, producing a separate output block for each, but instead produce a single output block for the whole target vector. This is because these methods are designated as class methods, which do not multicast. This is parallel to defining a static member function in a class in C++, taking a parameter that is a `std::vector` containing elements of that same class; that would be the natural way to represent this concept in C++, whereas in Eidos such methods are class methods that are called on the target vector but do not multicast. If this is gibberish to you, you can ignore it; the upshot is that it just works.

23.3.1 `output()`

The `output()` method is parallel to the `outputSample()` method of `Subpopulation` (see section 23.2.1), but allows output based upon any vector of genomes. Sample output for `output()`, abbreviated with ellipses:

```
#OUT: 10000 GS 10
Mutations:
9 187870 m1 1308 0 0.5 p2 9404 12
47 188084 m1 5994 0 0.5 p1 9415 12
...
Genomes:
p*:0 A 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23...
p*:1 A 0 1 2 3 4 5 6 68 7 8 9 69 10 12 13 14 15 16 17 18 19 20 21 22...
...
```

This is almost identical to the output from `outputSample()`, so see section 23.2.1 for further discussion. The main differences are in the header line. The output type here is `GS` (for "genomes, SLiM format"), and no subpopulation identifier is given since the genome vector being output may originate from more than one subpopulation. If the output is sent to a file with `output()`'s `filePath` option, the last field of the header provides the full path of the file to which the output was saved.

The other difference is in the genome identifiers in the Genomes section. Here, since the subpopulation of origin of the genomes is not known to `output()` – since it was just handed a vector of genomes that could have come from anywhere – the genome identifiers are of the form `p*:0`, `p*:1`, etc., with the * symbolizing an unknown source subpopulation. This syntax is intended to parallel the syntax used by SLiM's other output functions, to make it easier to share parsing code.

23.3.2 `outputMS()`

The `outputMS()` method is parallel to the `outputMSSample()` method of `Subpopulation` (see section 23.2.2), but allows output based upon any vector of genomes. Sample output for `outputMS()`, abbreviated with ellipses:

```
#OUT: 10000 GM 10
//
segsites: 165
positions: 0.1308131 0.4991499 0.5994599 0.6999700 0.9599960...
1101011011111001010000011111110000011101101100001111011110011100001 0...
1101011011111001010000011111110000011101101100001111011110011100001 0...
```

This is almost identical to the output from `outputMSSample()`, so see section 23.2.2 for further discussion. The differences are in the header line; output type `GM` is used here (representing "genomes, MS format"), and no subpopulation identifier is given since the genome vector being output may originate from more than one subpopulation.

The `outputMS()` method allows output to be sent to a file, with the optional `filePath` argument. In this case, the `#OUT:` header line is not emitted, since it would not be conformant with the MS data format specification.

23.3.3 `outputVCF()`

The `outputVCF()` method is parallel to the `outputVCFSample()` method of `Subpopulation` (see section 23.2.3), but allows output based upon any vector of genomes. Sample output for `outputVCF()`, abbreviated with ellipses:

```
#OUT: 10000 GV 20
##fileformat=VCFv4.2
##fileDate=20160613
##source=SLiM
##INFO=<ID=MID,Number=1,Type=Integer,Description="Mutation ID in SLiM">
##INFO=<ID=S,Number=1,Type=Float,Description="Selection Coefficient">
##INFO=<ID=DOM,Number=1,Type=Float,Description="Dominance">
##INFO=<ID=PO,Number=1,Type=Integer,Description="Population of Origin">
##INFO=<ID=GO,Number=1,Type=Integer,Description="Generation of Origin">
##INFO=<ID=MT,Number=1,Type=Integer,Description="Mutation Type">
##INFO=<ID=AC,Number=1,Type=Integer,Description="Allele Count">
##INFO=<ID=DP,Number=1,Type=Integer,Description="Total Depth">
##INFO=<ID=MULTIALLELIC,Number=0,Type=Flag,Description="Multiallelic">
##FORMAT=<ID=GT,Number=1,Type=String,Description="Genotype">
#CHROM POS ID REF ALT QUAL FILTER INFO FORMAT i0 i1 i2 i3 i4 i5...
1 1309 . A T 1000 PASS
MID=987550;S=0;DOM=0.5;PO=2;GO=9404;MT=1;AC=11;DP=1000 GT 0|1 0|0 0|1...
1 5995 . A T 1000 PASS
MID=987764;S=0;DOM=0.5;PO=1;GO=9415;MT=1;AC=11;DP=1000 GT 0|1 0|0 0|1...
...
```

This is almost identical to the output from `outputVCFSample()`, so see section 23.2.3 for further discussion. The differences are in the header line; type `GV` is used here (representing "genomes, VCF format"), and no subpopulation identifier is given since the genome vector being output may originate from more than one subpopulation. Also note that the sample size here is reported in genomes (i.e., `20`) whereas with `outputVCFSample()` it is reported in individuals (i.e., `10`). This is because this method operates on a vector of genomes, and thus that is the natural unit for the sample size. Nevertheless, since VCF output naturally groups genomes into diploid individuals, the target genome vector must have an even number of elements, and each pair of elements will be assumed to represent one individual.

The `outputVCF()` method allows output to be sent to a file, with the optional `filePath` argument. In this case, the `#OUT:` header line is not emitted, since it would not be conformant with the VCF data format specification.

23.4 SLiM additions to the `.trees` file format

The `.trees` files produced by the `treeSeqOutput()` method (section 21.12.2) are in a complex binary format, defined at the top level by the `kastore` library and at the next level by `msprime`; it is not documented here. Reading or writing compliant `.trees` files is a topic well beyond the scope of this manual. However, if the `pyslim.load()` method is used to load a `.trees` file into Python, the entities defined by the file, such as nodes, edges, and mutations, can then be accessed through the `pyslim` and `msprime` APIs in Python. Those entities often have a column for metadata, and this is where SLiM attaches its additional state information. The contents of those metadata fields is documented here. Directly using or generating this metadata information in Python is, again, beyond the scope of this manual, but the information provided here at least documents what you would need to know in order to do so. The `pyslim` package provides the more usual route to accessing this metadata information, and should suffice for the needs of almost all users.

This metadata is generally in a binary format. The descriptions below will give the number of bytes for each field, their C / C++ type, and a brief description.

23.4.1 Metadata for mutations

The derived state field for each mutation entry is actually a comma-separated list of mutation IDs, in ASCII, representing all of the stacked mutations present at the position in question after the addition (or removal) of a mutation; this is rather different from the way the derived state field is used in most `.trees` files.

Each mutation entry's metadata will then consist of a series of 16 byte metadata records, corresponding to the mutation IDs listed for the derived state:

4 bytes (`int32_t`): the id of the mutation type the mutation belongs to (i.e., `5` for `m5`)

4 bytes (`float`): the selection coefficient of the mutation

4 bytes (`int32_t`): the id of the subpopulation in which the mutation arose (i.e., `3` for `p3`)

4 bytes (`int32_t`): the simulation generation in which the mutation arose

Note that the same mutation ID may be described by multiple mutation entries, if differences in stacking or other factors lead to it being recorded multiple times. Furthermore, the metadata for these multiple descriptions may not match, since it is recorded at the time the mutation is added, and metadata such as the selection coefficient of a mutation can change as a mutation runs. When reading, SLiM will use the metadata associated with the last recorded version of each mutation.

23.4.2 Metadata for nodes

Each node will have 10 bytes of metadata attached:

8 bytes (`int64_t`): the SLiM genome ID for this node, as from `genomePedigreeID`

1 byte (`uint8_t`): true (`1`) if this node represents a null genome, as from `isNullGenome`

1 byte (`uint8_t`): the type of the genome (`0` for autosome, `1` for X, `2` for Y)

23.4.3 Metadata for individuals

Each individual will have 24 bytes of metadata attached:

8 bytes (`int64_t`): the SLiM pedigree ID for this individual, as from `pedigreeID`

4 bytes (`int32_t`): the age of this individual, as from `age`

4 bytes (`int32_t`): the subpopulation the individual belongs to (i.e., `3` for `p3`)

4 bytes (`int32_t`): the sex of the individual (`0` for female, `1` for male, `-1` for hermaphrodite)

4 bytes (`uint32_t`): flags; see below.

At present, only the low-order bit of the flags metadata, `0x01`, is used; if set, it indicates that this individual migrated between subpopulations during the current generation (following the `migrant` property of `Individual` described in section 21.6.1). Other flag bits are reserved and should be set to `0` until such time as they are defined.

The individual table also has a flags field, outside of the metadata record, and SLiM uses some bits in that field; that will be explained below since it is not part of the metadata record itself.

23.4.4 Metadata for populations

Each population will have 88 bytes of metadata attached at a minimum, followed by a variable number of 12-byte sections. The initial 88-byte section is structured as:

4 bytes (`int32_t`): the ID of this subpopulation, as from `id`

8 bytes (`double`): the selfing fraction (WF) or unused (nonWF)

8 bytes (`double`): the cloning fraction for females or hermaphrodites (WF) or unused (nonWF)

8 bytes (`double`): the cloning fraction for males or hermaphrodites (WF) or unused (nonWF)

8 bytes (`double`): the sex ratio as M:M+F (WF) or unused (nonWF)

8 bytes (`double`): spatial bounds `x0` value, unused in non-spatial models

8 bytes (`double`): spatial bounds `x1` value, unused in non-spatial models

8 bytes (`double`): spatial bounds `y0` value, unused in non-spatial models

8 bytes (`double`): spatial bounds `y1` value, unused in non-spatial models

8 bytes (`double`): spatial bounds `z0` value, unused in non-spatial models

8 bytes (`double`): spatial bounds `z1` value, unused in non-spatial models

4 bytes (`int32_t`): the number of migration records, as from `immigrantSubpopFractions`

The value of the last field above dictates the number of 12-byte metadata sections that follow, each of this format:

4 bytes (`int32_t`): the ID of the source subpopulation (i.e., `3` for `p3`)

8 bytes (`double`): the migration rate from the source subpopulation

23.4.5 The SLiM provenance table entry format

The provenance table is designed to hold an entry for each software program that has been involved in the creation of the file, providing a sort of "chain of custody" for the data in the file. For a `.trees` file to be openable in SLiM, there must be a provenance entry that indicates that the file was created by SLiM; it does not need to be the last entry, but the assumption is that any later entries represent software that understands how to preserve SLiM metadata conformance as described above. As long as the expected SLiM metadata format described above is strictly followed, the SLiM provenance may be spoofed to make a file openable in SLiM, too; this is what the `pyslim` package does, after attaching SLiM metadata. A SLiM provenance entry is an ASCII string, with no terminating `NULL` (the end of the string is dictated by the length of the entry itself, as tracked by kastore). A typical provenance table entry from SLiM 3.0 (`file_version` of `"0.1"`) looks like:

```
{"program":"SLiM", "version":"3.0", "file_version":"0.1",
    "model_type":"WF", "generation":1000, "remembered_node_count":0}
```

In SLiM 3.1 this has been extended to include more information (`file_version` of `"0.2"`). The new provenance table entry format provides a superset of the information in `file_version` `"0.1"` format, but some keys were renamed or moved within the JSON hierarchy. Nevertheless, backward compatibility should be possible if handled carefully. The new format looks like this:

```
{
    "environment": {
      "os": {
        "machine": "x86_64",
        "node": "anonymized.uoregon.edu",
        "release": "17.6.0",
        "system": "Darwin",
        "version": "Darwin Kernel Version 17.6.0: Tue May  8
          15:22:16 PDT 2018; root:xnu-4570.61.1~1/RELEASE_X86_64"
      }
    },
    "metadata": {
      "individuals": {
        "flags": {
          "16": {
            "description": "the individual was alive at the time the
              file was written",
            "name": "SLIM_TSK_INDIVIDUAL_ALIVE"
          },
          "17": {
            "description": "the individual was requested by the user
              to be remembered",
            "name": "SLIM_TSK_INDIVIDUAL_REMEMBERED"
          },
          "18": {
            "description": "the individual was in the first generation
              of a new population",
            "name": "SLIM_TSK_INDIVIDUAL_FIRST_GEN"
          }
        }
      }
    },
    "parameters": {
      "command": ["/usr/local/bin/slim", "-seed", "1", "~/test.slim"],
      "model": "initialize() {\n\tinitializeTreeSeq();
\n\tinitializeMutationRate(1e-7);\n\tinitializeMutationType(\"m1\", 0.5,
\"f\", 0.0);\n\tinitializeGenomicElementType(\"g1\", m1, 1.0);
\n\tinitializeGenomicElement(g1, 0, 99999);
\n\tinitializeRecombinationRate(1e-8);\n}\n1 {\n\tsim.addSubpop(\"p1\",
500);\n}\n2000 late() { sim.treeSeqOutput(\"~/Desktop/junk.trees\"); }\n",
      "model_type": "WF",
      "seed": 1
    },
    "schema_version": "1.0.0",
    "slim": {
      "file_version": "0.2",
      "generation": 2000,
    },
    "software": {
      "name": "SLiM",
      "version": "3.1"
    }
}
```

These provenance strings are a JSON strings (https://www.json.org). For SLiM 3.0, the keys must be provided in exactly the order given in the `file_version` `"0.1"` example above, including the exact positions of spaces and punctuation. For SLiM 3.1 and later, any JSON-compliant string supplying the expected keys will work, as a proper JSON reader has been incorporated into SLiM.

The top-level keys have the following meanings:

`environment`: This has information about the environment in which the simulation was executed. Right now it has an `os` key under it, with `machine`, `node`, `release`, `system`, and `version` keys under that, providing information vended by the POSIX function `uname()`. These keys are for diagnostic purposes, and are not particularly standardized, and should not be relied upon by reading software.

`metadata`: This has information about the metadata annotations used in the file. Right now it describes only the three bits that are used by SLiM in the `flags` column of the individuals table (*not* the flags field inside the metadata record for each individual). Further entries may be added describing all the metadata documented above.

`parameters`: This provides information that would be necessary to recreate the model run. The `command` key provides the command-line parameters (beginning with slim itself) that were used to run the model; for models run in SLiMgui this will be an empty array. The `model` key provides the script that was run by SLiM to generate the saved file; this is archived in the `.trees` file for easier identification and reproducibility of runs. Note that other files that may be sourced or read by the script are not archived; for full reproducibility it would be necessary to archive such auxiliary files alongside the `.trees` file. The script is a JSON-quoted string, so it should be un-JSON-quoted to reproduce the original script. The `file_version` key gives the version of the SLiM annotations in the file (provenance and metadata); at present only `"0.1"` and `"0.2"` are supported. The metadata format is the same for `"0.1"` and `"0.2"`; only the provenance format changed, as described here. The `model_type` key should be either `"WF"` or `"nonWF"`, depending upon the type of model that generated the file. This has some implications for the other metadata; in particular, some of the population metadata is required for WF models but unused in nonWF models, and individual ages in WF model data are expected to be `-1`. Finally, the `seed` key provides the original random number generator seed. If a seed is supplied at the command line with the `-s` option, that will be given here. Otherwise, the seed will be a randomly generated seed provided by SLiM. Note that this is only the original seed; if the seed is set in script using `setSeed()`, that will not be reflected here (but might be reflected in the script supplied by the `model` key).

`schema_version`: The version of the JSON schema used. The schema for provenance entries is documented at https://msprime.readthedocs.io/en/stable/provenance.html. Note that the schema is fairly minimal; most of the information emitted by SLiM is not described by it.

`slim`: This provides SLiM-specific information needed to correctly read `.trees` files into SLiM. The `file_version` key describes the overall version of the SLiM-specific information in the file, such as metadata and the provenance entry information itself, as outlined above. The `generation` key provides the generation at which the file was written, so that that generation can be restored when the file is read. The `remembered_node_count` key, which exists in `file_version` `"0.1"` files but not `file_version` `"0.2"` and later, specifies how many rows at the top of the nodes table are "remembered" by the user with the `treeSeqRememberIndividuals()` method; in `file_version` `"0.2"` and later, remembered individuals and genomes are controlled by the flags set on the rows of the individual table.

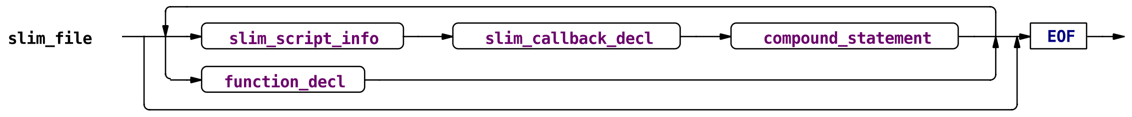
`software`: This provides information about the software program that produced this provenance entry. The `name` key gives the name of the software, and the `version` key gives the version number of the software. Note that in `file_version` `"0.1"` these were top-level keys instead, and the `name` key was called `program`, as illustrated by the `file_version` `"0.1"` example earlier.

With `file_version` `0.2`, the hope is that this existing provenance information will now be fairly stable, although further fields may be added.

24. SLiM extensions to the Eidos language

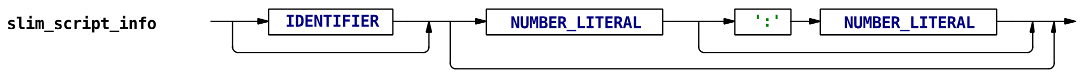
24.1 Extensions to the Eidos grammar

The Eidos language itself is defined by the grammar given in the Eidos manual. However, SLiM defines the grammar of a *SLiM input file*, which defines a small extension to the Eidos language – in particular, by using a different start rule than Eidos's interpreter normally uses:



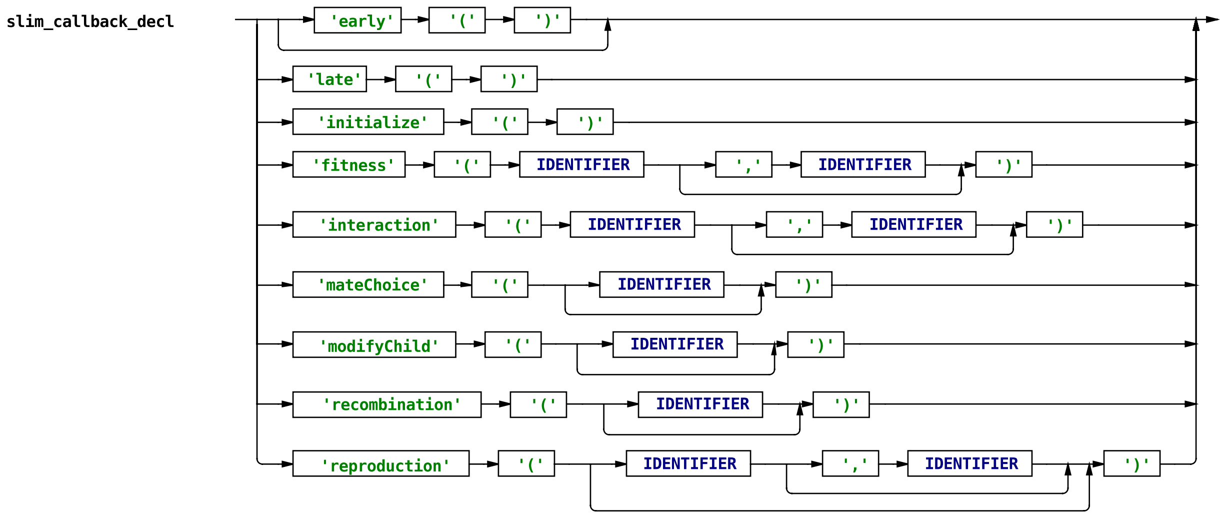
This start rule defines a SLiM input file as a series of zero or more *SLiM Eidos blocks*, each of which is a compound statement preceded by an informational section and a callback declaration. Definitions of user-defined Eidos functions may also be sprinkled in among those blocks. Note that ordinary Eidos statements are *not* allowed at the top level of the SLiM input file; they must be within the body of a SLiM Eidos block or a user-defined function. The SLiM input file therefore structures Eidos statements into encapsulated blocks.

In the definition of a SLiM Eidos block, the informational section is optional, since each of its components is optional; it looks like this:



The informational section begins with an optional identifier that can be used to later identify the script block programmatically. If supplied, it should be an identifier like `"s1"`, or more generally, `"sX"` where `X` is an integer greater than or equal to `0`. The rest of the informational section comprises an optional generation or range of generations in which the script block will be used by SLiM. The generation numbers are defined syntactically by the grammar as numeric literals, but semantically, there are further restrictions (see section 22.1).

The callback declaration section is also an addition by SLiM to the base Eidos grammar. It is also optional, since it can be empty:



This rule defines a SLiM script block as being one of the supported types of *Eidos event* or *Eidos callback* (`early()`, `late()`, `initialize()`, `fitness()`, `interaction()`, `mateChoice()`, `modifyChild()`, `recombination()`, or `reproduction()`). If no type specifier is provided, the script block is an `early()` event by default. The identifier tokens in this rule specify restrictions on the circumstances in which the callback will be used by SLiM. See chapter 22 for further details.

In all other respects the grammar of Eidos is unmodified in SLiM.

24.2 SLiM scoping rules

Eidos is largely a scopeless language; variables do not exist until they are defined, and once defined they continue to exist forever, unless/until they are subsequently undefined. The only exception to this, in Eidos, is that user-defined functions run within their own private scope. (See the Eidos manual for further discussion of scope in Eidos.)

SLiM, however, imposes some scoping rules upon the Eidos language. This occurs almost as a side effect of the way SLiM uses Eidos, albeit an intentional side effect. In particular, every call to a SLiM event or callback is run within a new Eidos interpreter, created solely for the purpose of running that particular invocation of that particular event or callback. These Eidos interpreters are torn down and thrown away as soon as the callout ends. Because of this, variables defined inside an event or callback have a scope that is limited to that callout; they will cease to exist as soon as the callout finishes.

This is actually desirable, in general, because it prevents the global namespace from becoming cluttered up with all of the local, temporary variables defined by particular events and callbacks. It also provides a clean way for SLiM to, in effect, pass values in to callbacks, as described in chapter 22. It mimics the scoping of languages like C and C++, albeit only at the level of whole functions/methods; even in SLiM there is no such thing as "block scope". In fact, this scoping behavior is identical to the way that user-defined functions in Eidos have their own private scope, and SLiM events and callbacks can actually be thought of as a special kind of user-defined function that is called automatically by SLiM, with a non-standard syntax for their declaration.

This design is not without drawbacks, however. The most obvious drawback is that in SLiM there isn't really such a thing as a global scope; there is *only* the local scope defined within events and callbacks. Only the special variables defined by SLiM, such as `sim`, possess the privileged status of being available everywhere (because SLiM sets them up before every callout).

SLiM provides some facilities to get around this problem. One such facility is the presence of `tag` properties on many of SLiM's classes, which can hold singleton `integer` values persistently (and the `tagF` property on some SLiM classes can hold singleton `float` values, as well). Another is the `setValue()`/`getValue()` facility provided by many of SLiM's classes, which allows persistent storage of arbitrarily named values that do not have to be singletons; this is much more flexible and open-ended than the `tag` facility, but is also not as fast or as easy to use.

The other way to keep a value persistently is to define it as a constant rather than a variable, using the Eidos function `defineConstant()`. In SLiM, the constants table is shared by all Eidos interpreters, and therefore constants defined in one event or callback are available in all subsequently executed code; SLiM's scoping rules do not apply to defined constants. For values that are in fact constant, this is straightforward and useful; SLiM models will often use `defineConstant()` to define constants related to population sizes, locus lengths, etc., in the `initialize()` callback of the model, and will then use those defined constants everywhere. Because even constants can be undefined with the `rm()` function, however, it is even possible to use this method to place non-constant values into the global namespace; when the value needs to change, simply remove the previous constant definition with `rm()` (with the optional parameter `removeConstants=T`); and then add a new constant definition with `defineConstant()`. This feels like a hack, since it violates the intended semantics of `defineConstant()`, but it is perfectly legal, and in some cases is a good solution to the global scope problem.

One thing that it is impossible to do in SLiM is to persistently keep values of `object` type. Values of `object` type cannot be placed into `tag` properties; they cannot be set as named values with `setValue()`; and they cannot be defined as constants with `defineConstant()`. The only `object` values that are persistent, in SLiM, are those set up by SLiM itself, such as `sim`. This is deliberate and necessary, because otherwise stale references to objects that no longer exist in the SLiM simulation could persist in variables. Since no persistent reference to an object can be created, stale references can never exist in a SLiM model, which greatly simplifies object lifetime management and error-checking issues. SLiM objects are only disposed of in between calls out to Eidos, at points in time when no Eidos reference to them can possibly exist because of the design of SLiM's scoping and persistence rules. See section 2.8.2 of the Eidos manual for further discussion.

25. SLiM reference sheet

This reference sheet may be downloaded as a separate PDF from http://messerlab.org/slim/.

Invoking SLiM at the command line:

```
slim -version | -usage | -testEidos | -testSLiM |
   [-seed <seed>] [-time] [-mem] [-Memhist] [-long] [-x] [-define <def>] <script file>
```

Types: `N:NULL, l:logical, i:integer, f:float, n:numeric, s:string, o<X>:object of class X`

Defining Eidos functions, events, and callbacks in a SLiM script:

`(ret-type)functionName(params) { ... }`	user-defined function
`[<id>] initialize() { ... }`	initialize() callback
`[<id>] [gen1 [: gen2]] [early()] { ... }`	early() Eidos event
`[<id>] [gen1 [: gen2]] late() { ... }`	late() Eidos event
`[<id>] [gen1 [: gen2]] fitness(<mutTypeId> [, <subpopId>]) { ... }`	fitness() callback
`[<id>] [gen1 [: gen2]] interaction(<intTypeId> [, <subpopId>]) { ... }`	interaction() callback
`[<id>] [gen1 [: gen2]] mateChoice([<subpopId>]) { ... } (WF)`	mateChoice() callback
`[<id>] [gen1 [: gen2]] modifyChild([<subpopId>]) { ... }`	modifyChild() callback
`[<id>] [gen1 [: gen2]] recombination([<subpopId>]) { ... }`	recombination() callback
`[<id>] [gen1 [: gen2]] reproduction([<subpopId> [, <sex>]]) ... (nonWF)`	reproduction() callback

SLiM globals:

```
  sim (o<SLiMSim>$)
  g1, ... (o<GEType>$)
  i1, ... (o<IntType>$)
  m1, ... (o<MutType>$)
  p1, ... (o<Subpop>$)
  s1, ... (o<SEBlock>$)
  self (o<SEBlock>$)
```

`fitness():`

```
  mut (o<Mutation>$)
  homozygous (l$)
  relFitness (f$)
  individual (o<Ind>$)
  genome1 (o<Genome>$)
  genome2 (o<Genome>$)
  subpop (o<Subpop>$)
```

`recombination():`

```
  individual (o<Ind>$)
  genome1 (o<Genome>$)
  genome2 (o<Genome>$)
  subpop (o<Subpop>$)
  breakpoints (i)
  gcStarts (i)
  gcEnds (i)
```

SLiMgui quick help:
opt-click on keyword

Code completion:
escape (ESC) or
cmd-period (⌘.)

`mateChoice():` (WF)

```
  individual (o<Ind>$)
  genome1 (o<Genome>$)
  genome2 (o<Genome>$)
  subpop (o<Subpop>$)
  sourceSubpop (o<Subpop>$)
  weights (f)
```

`reproduction():` (nonWF)

```
  individual (o<Ind>$)
  genome1 (o<Genome>$)
  genome2 (o<Genome>$)
  subpop (o<Subpop>$)
```

`modifyChild():`

```
  child (o<Ind>$)
  childGenome1 (o<Genome>$)
  childGenome2 (o<Genome>$)
  childIsFemale (l$)
  parent1 (o<Ind>$)
  parent1Genome1 (o<Genome>$)
  parent1Genome2 (o<Genome>$)
  isCloning (l$)
  isSelfing (l$)
  parent2 (o<Ind>$)
  parent2Genome1 (o<Genome>$)
  parent2Genome2 (o<Genome>$)
  subpop (o<Subpop>$)
  sourceSubpop (o<Subpop>$)
```

`interaction():`

```
  distance (f$)
  strength (f$)
  exerter (o<Ind>$)
  receiver (o<Ind>$)
  subpop (o<Subpop>$)
```

The sequence of events within one generation in WF models.

1. Execution of `early()` events
2. Generation of offspring:
   - 2.1. Choose source subpop
   - 2.2. Choose parent 1
   - 2.3. Choose parent 2 (`mateChoice()` callbacks)
   - 2.4. Generate the offspring (`recombination()` callbacks)
   - 2.5. Suppress/modify child (`modifyChild()` callbacks)
3. Removal of fixed mutations
4. Offspring become parents
5. Execution of `late()` events
6. Fitness value recalculation using `fitness()` callbacks
7. Generation count increment

The sequence of events within one generation in nonWF models.

1. Generation of offspring:
   - 1.1. Call `reproduction()` callbacks for individuals
   - 1.2. The callback(s) make calls requesting offspring
   - 1.3. Generate the offspring (`recombination()` callbacks)
   - 1.4. Suppress/modify child (`modifyChild()` callbacks)
2. Execution of `early()` events
3. Fitness value recalculation using `fitness()` callbacks
4. Viability/survival selection
5. Removal of fixed mutations
6. Execution of `late()` events
7. Generation count increment, individual age increments

Initialization functions (callable only from initialize() callbacks):

```
(void)initializeGeneConversion(n$ conversionFraction, n$ meanLength)
(void)initializeGenomicElement(io<GEType>$ genomicElementType, i$ start, i$ end)
(o<GEType>$)initializeGenomicElementType(is$ id, io<MutType> mutationTypes, n proportions)
(o<IntType>$)initializeInteractionType(is$ id, s$ spatiality, [l$ reciprocal],
      [n$ maxDistance], [s$ sexSegregation])
(void)initializeMutationRate(n rates, [Ni ends], [s$ sex])
(o<MutType>$)initializeMutationType(is$ id, n$ dominanceCoeff, s$ distributionType, ...)
(void)initializeRecombinationRate(n rates, [Ni ends], [s$ sex])
(void)initializeSex(s$ chromosomeType, [n$ xDominanceCoeff])
(void)initializeSLiMModelType(s$ modelType)
(void)initializeSLiMOptions([l$ keepPedigrees], [s$ dimensionality], [s$ periodicity],
      [i$ mutationRuns], [l$ preventIncidentalSelfing])
(void)initializeTreeSeq([l$ recordMutations], [f$ simplificationRatio],
      [l$ checkCoalescence], [l$ runCrosschecks])
```

SLiMSim:

```
chromosome => (o<Chromosome>$)
chromosomeType => (s$)
dimensionality => (s$)
dominanceCoeffX <–> (f$)
generation <–> (i$)
genomicElementTypes => (o<GEType>)
inSLiMgui => (l$) (deprecated in SLiM 3.2.1)
interactionTypes => (o<IntType>)
modelType => (s$)
mutationTypes => (o<MutType>)
mutations => (o<Mut>)
periodicity => (string$)
scriptBlocks => (o<SEBlock>)
sexEnabled => (l$)
subpopulations => (o<Subpop>)
substitutions => (o<Substitution>)
tag <–> (i$)
```

```
– (o<Subpop>$)addSubpop(is$ subpopID, i$ size, [f$ sexRatio])
– (o<Subpop>$)addSubpopSplit(is$ subpopID, i$ size, io<Subpop>$ sourceSubpop,
      [f$ sexRatio]) (WF)
– (i$)countOfMutationsOfType(io<MutType>$ mutType)
– (void)deregisterScriptBlock(io<SEBlock> scriptBlocks)
– (+)getValue(s$ key)
– (i)mutationCounts(No<Subpop> subpops, [No<Mut> mutations])
– (f)mutationFrequencies(No<Subpop> subpops, [No<Mut> mutations])
– (o<Mut>)mutationsOfType(io<MutType>$ mutType)
– (void)outputFixedMutations([Ns$ filePath], [l$ append])
– (void)outputFull([Ns$ filePath], [l$ binary], [l$ append], [l$ spatialPositions], [l$ ages])
– (void)outputMutations(o<Mut> mutations, [Ns$ filePath], [l$ append])
– (void)outputUsage(void)
– (i$)readFromPopulationFile(s$ filePath)
– (void)recalculateFitness([Ni$ generation])
– (o<SEBlock>$)register[Early/Late]Event(Nis$ id, s$ source, [Ni$ start], [Ni$ end])
– (o<SEBlock>$)registerFitnessCallback(Nis$ id, s$ source, Nio<MutType>$ mutType,
      [Nio<Subpop>$ subpop], [Ni$ start], [Ni$ end])
– (o<SEBlock>$)registerInteractionCallback(Nis$ id, s$ source, io<IntType>$ intType,
      [Nio<Subpop>$ subpop], [Ni$ start], [Ni$ end])
– (o<SEBlock>$)register[MateChoice (WF)/ModifyChild/Recombination]Callback(Nis$ id, s$ source,
      [Nio<Subpop>$ subpop], [Ni$ start], [Ni$ end])
– (o<SEBlock>$)registerReproductionCallback(Nis$ id, s$ source, [Nio<Subpop>$ subpop],
      [Ns$ sex], [Ni$ start], [Ni$ end]) (nonWF)
– (o<SEBlock>$)rescheduleScriptBlock(o<SEBlock>$ block, [Ni$ start], [Ni$ end],
      [Ni generations])
– (void)setValue(s$ key, + value)
– (void)simulationFinished(void)
– (l$)treeSeqCoalesced(void)
– (void)treeSeqOutput(s$ path, [l$ simplify])
– (void)treeSeqRememberIndividuals(o<Ind> individuals)
– (void)treeSeqSimplify(void)
```

Subpopulation (Subpop):

```
cloningRate => (f) (WF)
firstMaleIndex => (i$)
fitnessScaling <–> (f$)
genomes => (o<Genome>)
id => (i$)
immigrantSubpopFractions => (f) (WF)
immigrantSubpopIDs => (i) (WF)
individualCount => (i$)
individuals => (o<Ind>)
selfingRate => (f$) (WF)
sexRatio => (f$) (WF)
spatialBounds => (f)
tag <–> (i$)
```

```
– (No<Ind>$)addCloned(o<Ind>$ parent) (nonWF)
– (No<Ind>$)addCrossed(o<Ind>$ parent1, o<Ind>$ parent2, [Nfs$ sex]) (nonWF)
– (No<Ind>$)addEmpty([Nfs$ sex]) (nonWF)
– (No<Ind>$)addRecombinant(No<Genome>$ strand1, No<Genome>$ strand2, Ni breaks1,
     No<Genome>$ strand3, No<Genome>$ strand4, Ni breaks2, [Nfs$ sex]) (nonWF)
– (No<Ind>$)addSelfed(o<Ind>$ parent) (nonWF)
– (f)cachedFitness(Ni indices)
– (void)configureDisplay([Nf center], [Nf$ scale], [Ns$ color])
– (void)defineSpatialMap(s$ name, s$ spatiality, Ni gridSize, f values, [l$ interpolate],
     [Nf valueRange], [Ns colors])
– (+)getValue(s$ key)
– (void)outputMSSample(i$ sampleSize, [l$ replace], [s$ requestedSex],
     [Ns$ filePath], [l$ append], [l$ filterMonomorphic])
– (void)outputSample(i$ sampleSize, [l$ replace], [s$ requestedSex],
     [Ns$ filePath], [l$ append])
– (void)outputVCFSample(i$ sampleSize, [l$ replace], [s$ requestedSex],
     [l$ outputMultiallelics], [Ns$ filePath], [l$ append])
– (l)pointInBounds(f point)
– (f)point[Periodic|Reflected|Stopped](f point)
– (f)pointUniform([i$ n])
– (void)removeSubpopulation(void) (nonWF)
– (void)sampleIndividuals(i$ size, [l$ replace], [No<Ind>$ exclude], [Ns$ sex], [Ni$ tag],
     [Ni$ minAge], [Ni$ maxAge], [Nl$ migrant])
– (void)setCloningRate(n rate) (WF)
– (void)setMigrationRates(io<Subpop> sourceSubpops, n rates) (WF)
– (void)setSelfingRate(n$ rate) (WF)
– (void)setSexRatio(f$ sexRatio) (WF)
– (void)setSpatialBounds(f bounds)
– (void)setSubpopulationSize(i$ size) (WF)
– (void)setValue(s$ key, + value)
– (s)spatialMapColor(s$ name, f value)
– (f$)spatialMapValue(s$ name, f point)
– (void)subsetIndividuals([No<Ind>$ exclude], [Ns$ sex], [Ni$ tag], [Ni$ minAge],
     [Ni$ maxAge], [Nl$ migrant])
– (void)takeMigrants(o<Ind> migrants) (nonWF)
```

Chromosome:

```
colorSubstitution <–> (s$)
geneConversionFraction <–> (f$)
geneConversionMeanLength <–> (f$)
genomicElements => (o<GElement>)
lastPosition => (i$)
mutationEndPositions[F|M] => (i)
mutationRates[F|M] => (f)
overallMutationRate[F|M] => (f$)
overallRecombinationRate[F|M] => (f$)
recombinationEndPositions[F|M] => (i)
recombinationRates[F|M] => (f)
tag <–> (i$)
```

```
– (integer)drawBreakpoints([No<Ind>$ parent], [Ni$ n])
– (void)setMutationRate(n rates, [Ni ends], [s$ sex])
– (void)setRecombinationRate(n rates, [Ni ends], [s$ sex])
```

Individual (Ind):

```
age <–> (i$) (nonWF)
color <–> (s$)
fitnessScaling <–> (f$)
genomes => (o<Genome>)
genome1 => (o<Genome>$)
genome2 => (o<Genome>$)
index => (i$)
migrant => (l$)
pedigreeID => (i$)
pedigreeParentIDs => (i)
pedigreeGrandparentIDs => (i)
sex => (s$)
spatialPosition => (f)
subpopulation => (o<Subpop>$)
tag <–> (i$)
tagF <–> (f$)
uniqueMutations => (o<Mut>)
x <–> (f$)
y <–> (f$)
z <–> (f$)
```

```
– (l)containsMutations(o<Mut> mutations)
– (i$)countOfMutationsOfType(io<MutType>$ mutType)
– (+)getValue(s$ key)
– (f)relatedness(o<Ind> individuals)
+ (void)setSpatialPosition(f position)
– (void)setValue(s$ key, + value)
– (f$)sumOfMutationsOfType(io<MutType>$ mutType)
– (o<Mut>)uniqueMutationsOfType(io<MutType>$ mutType)
```

Genome:

```
genomePedigreeID => (i$)
genomeType => (s$)
isNullGenome => (l$)
mutations => (o<Mut>)
tag <–> (i$)
```

```
+ (void)addMutations(o<Mut> mutations)
+ (o<Mut>)addNewDrawnMutation(io<MutType> mutationType, i position, [Ni originGeneration],
      [Nio<Subpop> originSubpop])
+ (o<Mut>)addNewMutation(io<MutType> mutationType, n selectionCoeff, i position,
      [Ni originGeneration], [Nio<Subpop> originSubpop])
– (l$)containsMarkerMutation(io<MutType>$ mutType, i$ position, [l$ returnMutation])
– (l)containsMutations(o<Mut> mutations)
– (i$)countOfMutationsOfType(io<MutType>$ mutType)
– (o<Mut>)mutationsOfType(io<MutType>$ mutType)
+ (void)output([Ns$ filePath], [l$ append])
+ (void)outputMS([Ns$ filePath], [l$ append], [l$ filterMonomorphic])
+ (void)outputVCF([Ns$ filePath], [l$ outputMultiallelics], [l$ append])
– (i)positionsOfMutationsOfType(io<MutType>$ mutType)
+ (void)removeMutations([No<Mut> mutations], [l$ substitute])
– (f$)sumOfMutationsOfType(io<MutType>$ mutType)
```

Mutation (Mut):

```
id => (i$)
mutationType => (o<MutType>$)
originGeneration => (i$)
position => (i$)
selectionCoeff => (f$)
subpopID <–> (i$)
tag <–> (i$)
```

```
– (+)getValue(s$ key)
– (void)setMutationType(io<MutType>$ mutType)
– (void)setSelectionCoeff(f$ selectionCoeff)
– (void)setValue(s$ key, + value)
```

Substitution:

```
id => (i$)
fixationTime => (i$)
mutationType => (o<MutType>$)
originGeneration => (i$)
position => (i$)
selectionCoeff => (f$)
subpopID <–> (i$)
tag <–> (i$)
```

```
– (+)getValue(s$ key)
– (void)setValue(s$ key, + value)
```

MutationType (MutType):

```
color <–> (s$)
colorSubstitution <–> (s$)
convertToSubstitution <–> (l$)
distributionParams => (f)
distributionType => (s$)
dominanceCoeff <–> (f$)
id => (i$)
mutationStackGroup <–> (i$)
mutationStackPolicy <–> (s$)
tag <–> (i$)
```

```
– (+)getValue(s$ key)
– (void)setDistribution(s$ distType, ...)
– (void)setValue(s$ key, + value)
```

Fitness effects of mutations:

no mutation present	1
heterozygote	1 + *h***s*
homozygote	1 + *s*

s = `mut.selectionCoeff`
h = `mutType.dominanceCoeff`

SLiMgui: (in SLiMgui only)

```
pid => (i$)
```

```
– (void)openDocument(s$ filePath)
– (void)pauseExecution(void)
```

GenomicElement (GElement):

```
endPosition => (i$)
genomicElementType => (o<GEType>$)
startPosition => (i$)
tag <–> (i$)
```

```
– (void)setGenomicElementType(io<GEType>$ genomicElementType)
```

GenomicElementType (GEType):

```
color <–> (s$)
id => (i$)
mutationFractions => (f)
mutationTypes => (o<MutType>)
tag <–> (i$)
```

```
– (+)getValue(s$ key)
– (void)setMutationFractions(io<MutType> mutationTypes, n proportions)
– (void)setValue(s$ key, + value)
```

SLiMEidosBlock (SEBlock):

```
active <–> (i$)
end => (i$)
id => (i$)
source => (s$)
start => (i$)
tag <–> (i$)
type => (s$)
```

InteractionType (IntType):

```
id => (i$)
maxDistance <–> (f$)
reciprocal => (l$)
sexSegregation => (s$)
spatiality => (s$)
tag <–> (i$)
```

```
– (f)distance(o<Ind> individuals1, [No<Ind> individuals2])
– (f)distanceToPoint(o<Ind> individuals1, f point)
– (o<Ind>)drawByStrength(o<Ind>$ individual, [i$ count])
– (void)evaluate([No<Subpop> subpops], [l$ immediate])
– (+)getValue(s$ key)
– (i)interactingNeighborCount(o<Ind> individuals)
– (f)interactionDistance(o<Ind> individuals1, [No<Ind> individuals2])
– (o<Ind>)nearestInteractingNeighbors(o<Ind>$ individual, [i$ count])
– (o<Ind>)nearestNeighbors(o<Ind>$ individual, [i$ count])
– (o<Ind>)nearestNeighborsOfPoint(o<Subpop>$ subpop, f point, [i$ count])
– (void)setInteractionFunction(s$ functionType, ...)
– (void)setValue(s$ key, + value)
– (f)strength(o<Ind>$ receiver, [No<Ind> exerters])
– (f)totalOfNeighborStrengths(o<Ind> individuals)
– (void)unevaluate(void)
```

26. Revision history

This is a history of the revisions of SLiM since version 2.0. It focuses on new features, not bug fixes (which rapidly become ancient history), and it does not contain every detail. The `VERSIONS` file in the SLiM source code provides more detail, including changes that might not be user-visible at all. Beyond that, the commit history in GitHub is of course the definitive history of the project. For those wanting a quick overview of SLiM's history, however, this is a good place to start.

Version 3.2.1

Feature: `drawBreakpoints()` method on `Chromosome` to draw breakpoints using SLiM's logic
Feature: `rbeta()` function in Eidos for draws from a beta distribution
Feature: `pnorm()` function in Eidos for the CDF of the normal distribution
Feature: new `SLiMgui` class, with an instance named `slimgui`, available only under SLiMgui
Feature: `SLiMgui.openDocument()` method to open a file in SLiMgui from script
Feature: `SLiMgui.pauseExecution()` method to pause a running SLiMgui simulation from script
Feature: `SLiMgui.pid` property to get the process ID of SLiMgui from script
Feature: `Subpopulation.configureDisplay()` method to customize SLiMgui display of subpops
Tweak: revised recipes 13.11 and 13.17 to use the new SLiMgui class
Tweak: `slim` (the command-line tool) can now read its script from `stdin` (i.e., from a pipe)
Tweak: new recipe 15.15 (Implementing a Wright–Fisher model with a nonWF model)
Tweak: new recipe 15.16 (Alternation of generations)
Tweak: added support for `make install` with `cmake`, thanks to Peter Ralph
Tweak: added support for link-time optimization (LTO), thanks to Kevin Thornton
Tweak: improved the reseeding procedure in recipes 10.2, 10.3, 10.6.2, and 16.3
Tweak: SLiMgui should now run on macOS 10.10 and later (formerly 10.11 and later)
Policy change: `inSLiMgui` property of `SLiMSim` deprecated; use `exists("slimgui")`
Bug fix: `setValue()` did not copy the value, allowing corruption of the set value in rare cases
Bug fix: calling `deregisterScriptBlock()` more than once on the same block did bad things
Bug fix: the `pedigreeGrandparentIDs` property returned incorrect values
Bug fix: loading a `.trees` file with a mismatched chromosome length now gives an error
Bug fix: SLiMgui crash when displaying a large number of genomic element types
Bug fix: code completion bug when completing off a base of return/else/do/in
Bug fix: fixed poor error-reporting for malformed command-line definitions
Bug fix: fixed a raise that would crash SLiMgui, triggered by an illegal numeric constant in script

Version 3.2

Feature: keyword-based "Find Recipe…" panel in SLiMgui to make recipe lookup easier
Feature: code completion in SLiMgui is now much smarter (`iTR -> initializeTreeSeq()`, e.g.)
Feature: memory usage summary in SLiMgui's profile, also from new `outputUsage()` method
Feature: `usage()` function in Eidos to get the current / peak total memory usage
Feature: `addRecombinant()` method for nonWF for horizontal gene transfer, haploid models, etc.
Feature: `rgeom()` function in Eidos for draws from a geometric distribution
Feature: button in SLiMgui's output area to view/change the current working directory
Feature: `outputMS()` and `outputMSSample()` can now filter out in-sample-monomorphic sites
Feature: new color-palette functions `heatColors()`, `rainbow()`, `terrainColors()`, `cmColors()`

Tweak: new recipe 15.13, modeling clonal haploids in nonWF models with `addRecombinant()`
Tweak: new recipe 15.14, modeling clonal haploid bacteria with horizontal gene transfer
Tweak: vectorized the Eidos color-manipulation functions, using matrix arguments/returns
Tweak: add a `[print=T]` flag to `version()` so switching on version can avoid unwanted output
Tweak: vectorized the `exists()` function so a vector of symbols can be checked in one call
Tweak: some minor optimization work, especially on property / method dispatch in Eidos
Policy change: `asString(NULL)` now returns `"NULL"` for easier output generation
Policy change: string concatenation with `+` now adds `"NULL"` for `NULL`, for easier output
Policy change: scheduling an event/callback into the past now produces an error
Bug fix: fixed a major performance issue for large nonWF models with a lot of genetic diversity
Bug fix: recipe 11.1 issue with the `calcFST()` function returning `NAN` in some marginal cases
Bug fix: code completion in SLiMgui after `return`, `in`, `else`, and `do` now works correctly
Bug fix: many Eidos functions are now more robust to being passed `NAN` (e.g., `rpois()` hang)
Bug fix: corrupted spatial location data for some individuals in `.trees` files
Bug fix: minor issue with SLiMgui's population visualization graph's migration rate arrows
Bug fix: symbol table bug that would bite models defining a very large number of symbols
Bug fix: crash in `addEmpty()` that nobody noticed because nobody uses it
Bug fix: incorrect `modifyChild()` source subpop when using `addCloned()/Crossed()/Selfed()`
Bug fix: incorrect `isCloning/isSelfing` in `modifyChild()` when using `addCloned()/addSelfed()`
Bug fix: incorrect `parent2` values in `modifyChild()` in clonal models (shouldn't be used anyway)

Version 3.1

Feature: greatly increased the performance of spatial interactions with large population size
Feature: added `interactionDistance()` method to get interaction-conditional distances
Feature: added `nearestInteractingNeighbors()` to get interaction-conditional neighbors
Feature: added `interactingNeighborCount()` to count interaction-conditional neighbors
Feature: `rememberIndividuals()` now actually remembers individuals (as well as genomes)
Feature: added automatic remembering of the initial generation, for easier recapitation
Feature: `dmvnorm()` added to Eidos to get probability densities from a multivariate normal dist.
Tweak: extended the `.trees` provenance format for better reproducibility / self-documentation
Tweak: new recipe 13.19, biased gene conversion (two recipes actually)
Tweak: improved recipe 13.4 (reading MS format files), with big performance benefits for it
Tweak: updated all chapter 16 recipes (tree-sequence recording) to reflect changes
Policy change: `strength()` now requires a singleton first argument, `receiver`
Policy change: `.trees` files now have their time rebased to msprime-style times on save
Policy change: `initializeInteractionType()` now warns if no maximum distance is given
Bug fix: memory leak with cycling/varying subpopulation size (genome recycling bug)
Bug fix: nodes in `.trees` files occasionally being marked as null genomes incorrectly
Bug fix: incorrect fitness in WF models using only `fitnessScaling` to modify fitness

Version 3.0

Feature: non-Wright-Fisher (nonWF) models, chosen with `initializeSLiMModelType()`
Feature: nonWF additions (`age`, `addX()` methods, `takeMigrants()`, `removeSubpopulation()`)
Feature: nonWF additions (`reproduction()` callbacks, `registerReproductionCallback()`)

Feature: new `sampleIndividuals()` and `subsetIndividuals()` methods on `Subpopulation`
Feature: new `fitnessScaling` property on `Subpopulation` and `Individual` to alter fitness
Feature: tree-sequence recording, enabled with `initializeTreeSeq()`
Feature: tree-sequence recording additions (`treeSeqX()` methods)
Feature: new `seqLen()` function in Eidos to generate a zero-based sequence of a given length
Feature: new `getwd()` / `setwd()` functions in Eidos to get and change the working directory
Feature: new `var()` / `cov()` / `cor()` stats functions in Eidos for variance / covariance / correlation
Feature: new `rcauchy()` function for Cauchy distribution (also new interaction function, "c")
Feature: new `genome1` and `genome2` properties on Individual for easier haploid models etc.
Feature: new `migrant` property on Individual, usable in both WF and nonWF models
Feature: display interaction types in SLiMgui's drawer, with hover preview for the function
Feature: improved subpopulation display options in SLiMgui, including spatial map choice
Feature: increase maximum chromosome length from `1e9` to `1e15`
Feature: code completion in SLiMgui can now supply argument names when in a call
Feature: added `getValue()` / `setValue()` functionality to `Substitution`
Feature: optimization work across SLiM and Eidos
Tweak: new recipes for nonWF (chapter 15) and tree-sequence recording (chapter 16)
Tweak: new recipe 13.3 III (mortality-based fitness using `fitnessScaling`)
Tweak: new recipe 13.18 (modeling opposite ends of a chromosome)
Tweak: recipe fixes to conform with changes (13.1, 13.2, 13.9, 13.13, 11.2)
Tweak: `mean()` now works with a logical vector argument
Tweak: vectorize point-processing methods (`pointX()`, `setSpatialPosition()`)
Tweak: add `removeMutations(NULL)` option to quickly remove all mutations from a `Genome`
Tweak: add `[returnMutation = F]` argument to `containsMarkerMutation()` to get the mutation
Tweak: new `suppressWarnings()` function in Eidos to… suppress warnings
Policy change: return values are no longer implied by the value of the last statement
Policy change: `void` is now a true value type in Eidos, not a synonym for `NULL`
Policy change: property/method accesses on zero-length vectors now raise if ambiguous in type
Policy change: `cachedFitness()` may no longer be called from a `late()` event in WF models
Policy change: the default working directory when running in SLiMgui is now `~/Desktop`
Bug fix: incorrect strengths from `InteractionType` with periodic boundaries
Bug fix: gene conversion rate of exactly 1.0 would be treated as 0.0
Bug fix: crash when `setSubpopulationSize(0)` was called twice on the same subpop
Bug fix: crash with the "fitness over time" graph in SLiMgui with an invalid simulation
Bug fix: rare crash on quit in SLiMgui
Bug fix: crash due to stack overflow with large population size and callbacks
Bug fix: display glitch in SLiMgui on Retina displays
Bug fix: fix incorrect actual recombination rate for specified rate of `0.5`, impose `<= 0.5` limit
Bug fix: `rdunif()` can now generate draws over the full 64-bit range, not limited to 32-bit
Bug fix: crash in SLiMgui displaying haplotypes in a model with null genomes (X/Y models)
Bug fix: dropped model output from just before a simulation terminates due to an error

Version 2.6

Feature: Eidos now supports matrices (2-D) and arrays (*n*-D), with new related functions

Feature: haplotype plots and haplotype-based chromosome view display mode
Feature: periodic spatial boundary conditions now supported, including in `InteractionType`
Feature: visualize `MutationType` DFEs in the info drawer in SLiMgui (hover the mouse to see)
Feature: new `rdunif()` Eidos function for draws from discrete uniform distributions
Feature: new `rmvnorm()` Eidos function for draws from multivariate normal distributions
Feature: optimizations of the Eidos core may lead to ~20% speedup for Eidos-intensive models
Tweak: the `apply()` function is now renamed `sapply()`, following R
Tweak: increased display flexibility of individual mutation types in the chromosome view
Tweak: the number of bins in the frequency spectrum plot in SLiMgui can now be changed
Tweak: improved display of mutation/recombination maps in SLiMgui, with a broader range
Tweak: `addNew[Drawn]Mutation()` are now vectorized for speed when adding many mutations
Tweak: new `positionsOfMutationsOfType()` method on `Genome` for speed of some models
Tweak: extended the `integer()` function of Eidos to be able to create two-valued filled vectors
Tweak: `defineSpatialMap()` now accepts a matrix/array of values (backward compatible)
Tweak: `sapply()` (which was `apply()`) has a new `simplify` parameter to get a matrix/array result
Tweak: extended recipe 13.5 to show off the new haplotype display options, check it out
Tweak: revised recipe 13.9 (tracking true local ancestry) for much greater speed
Tweak: recipe 13.12 (modeling nucleotides) is now much faster, with optimizations in SLiM
Tweak: added recipes 13.15 (modeling microsatellites) and 13.16 (modeling transposons)
Tweak: added recipe 13.17: multiple QTL-based quantitative phenotypic traits with pleiotropy
Tweak: added recipe 14.12 to demonstrate periodic boundary conditions in spatial models
Tweak: revised recipes to use `sapply()` instead of `apply()`, other minor recipe tweaks
Policy change: assignment into a subset of a property is no longer legal in Eidos (you don't care)
Policy change: `version()` now returns a numeric version number, for runtime version checking
Policy change: `Chromosome` properties that are undefined now raise when accessed
Policy change: `addNew[Drawn]Mutation()` returns requested mutations whether added or not
Policy change: `periodicity` inserted in `initializeSLiMOptions()`; use named arguments there!
Bug fix: possible incorrect mutation freqs/counts after `addMutations()` / `removeMutations()`
Bug fix: fixed a long-standing display bug in SLiMgui with added/removed mutations
Bug fix: very minor bug fixes in `doCall()`, SLiMgui, etc.; very unlikely impact on model results

Version 2.5

Feature: add support for user-defined Eidos functions in SLiM – make your own functions
Feature: support for variable mutation rate along the chromosome (i.e., "hot" and "cold" spots)
Feature: display of the mutation-rate map in SLiMgui with the R button
Feature: `Mutation` now supports the `getValue()`/`setValue()` mechanism
Feature: SLiMgui can do script prettyprinting, for nice code formatting
Feature: new ternary conditional operator, `?else`, added to Eidos, like `?:` in C/C++
Feature: support for block-style `/* */` comments added to Eidos, as in C/C++
Feature: added a function `source()` to read in and execute Eidos code from a given file
Feature: the SLiM and Eidos documentation now has hyperlinks in its table of contents
Major bug fix: new mutations were not added correctly in clonal reproduction, in 2.4–2.4.2
Tweak: improved `pmax()`, `pmin()`, `max()`, `min()`, `range()`, `seq()`, `any()`, `all()`, `unique()`
Tweak: added a `sumExact()` function to Eidos for exact summation of floating-point numbers

Tweak: fixed a bug in recipe 11.1's F_{ST} calculation code, and split it into a standalone function
Tweak: added recipe 13.13, illustrating how to make a simple haploid clonal model in SLiM
Tweak: added recipe 13.14, modeling variation in functional density along the chromosome
Policy change: removed the `mutationRate` property of `Chromosome` in favor of new API
Policy change: `function()`, `method()`, `property()` renamed to `functionSignature()`, etc.
Policy change: argument `function` for `doCall()` renamed to `functionName`
Bug fix: improved numerical accuracy for complex recombination maps
Bug fix: incorrect results from InteractionType if individuals had an identical coordinate value

Version 2.4.2

Major bug fix: fix non-unique mutation id bug (incorrect output from many/most models)

Version 2.4.1

Bug fix: fix stale subpop pointer bug (possible crash or incorrect data in multi-subpop sims)

Version 2.4

Feature: extensive internal optimizations for better performance of many models
Feature: model runtime profiling added in SLiMgui for performance evaluation
Feature: `sumOfMutationsOfType()` method added for fast QTL effect addition
Feature: `preventIncidentalSelfing` option added to `initializeSLiMOptions()`
Feature: optionally configure the mutation run count in `initializeSLiMOptions()`
Feature: `system()` function to call out to Unix to run commands
Feature: added PDF viewing to SLiMgui for R plotting integration (see recipe 13.11)
Feature: chromosome view display customization via right-click in SLiMgui
Feature: population view display customization via right-click in SLiMgui
Feature: `writeTempFile()` function for creating randomly named temporary files
Feature: new `catn()` and `paste0()` functions for simpler output generation
Feature: `MutationType`, `GenomicElementType`, `InteractionType` now support `get/setValue()`
Feature: add `mutationStackGroup` property to `MutationType` and improve stacking options
Major bug fix: significant bug in the Eidos function `setDifference()` (no impact if not using it)
Tweak: added top/bottom splitview in SLiMgui to allow greater display flexibility
Tweak: the play speed slider in SLiMgui now shows the chosen play speed in a tooltip
Tweak: added font size preference in SLiMgui for presentations, etc.
Tweak: new `inSLiMgui` property on `SLiMSim` to tell whether the model is running in SLiMgui
Tweak: `rescheduleScriptBlock()` method added on `SLiMSim` for easier block rescheduling
Tweak: `ttest()` function added for performing *t*-tests in Eidos
Tweak: added `–l` (`–long`) command-line option for more verbose output
Policy change: scripted (type "s") DFEs in `MutationType` now have access to SLiM constants
Bug fix: `for` loops on `seqAlong()` vectors with a zero-length parameter were incorrect

Version 2.3

Feature: continuous space (1D, 2D, or 3D) and spatial positions for `Individual` (`x`, `y`, and `z`)
Feature: landscape maps that can define environmental values across space
Feature: interactions (both non-spatial and spatial), including `interaction()` callbacks
Feature: "global" `fitness()` callbacks that are called once for every individual
Tweak: `outputFull()` and `readFromPopulationFile()` now save/restore spatial positions

Tweak: `mateChoice()` callbacks can now return a vector of all zero to reject the first parent
Tweak: `mateChoice()` callbacks can now return a singleton `Individual` as the chosen parent
Tweak: added several color-conversion functions to Eidos (RGB to/from HSV, etc.)
Policy change: `readFromPopulationFile()` no longer recalculates fitness values
Policy change: `readFromPopulationFile()` now warns if called outside a `late()` event

Version 2.2.1

Feature: SLiMgui is now a proper document-based app using the `.slim` file extension
Feature: `tagF` property on `Individual` for storage of `float` custom state
Feature: `order()` function that provides sorting indices, like the R `order()` function
Feature: custom coloring of individuals, etc., in SLiMgui using new `color` properties
Tweak: SLiMgui's recycle button now highlights green when the script has been changed
Tweak: arbitrary Eidos expressions are now legal in command-line constant definitions
Policy change: multiple calls to `initializeRecombinationRate()` is now explicitly illegal

Version 2.2

Feature: `recombination()` callbacks allow scripted alteration of recombination breakpoints
Feature: `containsMarkerMutation()` method allows fast checking for "marker" mutations
Feature: `clock()` function gives the CPU usage of the process, for measuring performance
Feature: `setValue()` / `getValue()` methods provide several classes with dictionary-like values
Feature: command-line constant definition using a `–define` or `–d` flag passed to `slim`
Tweak: "tips & tricks" panel for SLiMgui that introduces some obscure features of the app

Version 2.1.1

Feature: `mutationCounts()` method provides raw mutation reference counts

Version 2.1

Feature: `Individual` class added to represent individuals, with many associated changes
Feature: optional pedigree-based relatedness tracking for individuals
Feature: overhaul of SLiM output methods to provide file-based output and appending
Feature: new `Genome` output methods allow output of custom samples
Feature: VCF format output added to the existing SLiM and MS formats
Feature: `Mutation` now has a unique identifier usable for tracking mutations through time
Feature: `Mutation` and `Substitution` now have a `tag` property like many other SLiM classes
Feature: DFE type `"s"` now allows scripted DFEs for `MutationType`
Feature: sex-specific recombination rates and/or recombination maps
Feature: default arguments and named arguments supported for Eidos functions and methods
Feature: `deleteFile()` and `createDirectory()` functions added to Eidos
Feature: set operation functions (union, intersection, etc.) added to Eidos
Tweak: `size()` method added to the Eidos object base class
Tweak: recipes now openable directly from the Recipes submenu in SLiMgui
Policy change: output of mutations now includes a mutation identifier field (format change)
Policy change: `readFromPopulationFile()` now sets the generation as a side effect
Policy change: class methods in Eidos now provide non-multicasted method invocation
Policy change: `addNewMutation()` and `addNewDrawnMutation()` changed to class methods

Version 2.0.4

Minor bug fixes.

Version 2.0.3

Minor bug fixes.

Version 2.0.2

Feature: binary format for `outputFull()`, for smaller files and much faster save/load

Feature: `setMutationType()` added to allow mutations to be assigned to a different type

Feature: `beep()` function allows audible output from scripts

Tweak: `readFromPopulationFile()` can now read the new binary file format

Version 2.0.1

Feature: `format()` function added to Eidos for customized formatting of output

Version 2.0

This was the original version of SLiM 2, which was an almost complete rewrite of SLiM and introduced such major features as Eidos and SLiMgui. The full list of changes is far too extensive to detail here. Before SLiM 2 came SLiM 1, which was documented in Messer (2013).

27. Credits and licenses for incorporated software

SLiM incorporates code from various other software frameworks and packages. This section provides credit and license information for the software thus incorporated, as well as for SLiM itself.

27.1 SLiM

SLiM is free software: you can redistribute it and/or modify it under the terms of the GNU General Public License as published by the Free Software Foundation, either version 3 of the License, or (at your option) any later version.

SLiM is distributed in the hope that it will be useful, but WITHOUT ANY WARRANTY; without even the implied warranty of MERCHANTABILITY or FITNESS FOR A PARTICULAR PURPOSE. See the GNU General Public License for more details.

You should have received a copy of the GNU General Public License along with SLiM. If not, see http://www.gnu.org/licenses/.

27.2 GNU Scientific Library (GSL)

SLiM contains a modified distribution of the GNU Scientific Library (GSL), which is also licensed under the GNU General Public License under the same terms stated above. Thanks to the authors of the GSL for their very useful software, which can be found in full form at http://www.gnu.org/software/gsl/.

27.3 kastore / msprime

SLiM contains code from the msprime and kastore software packages (enabling the tree-sequence recording feature of SLiM 3, and the ability to save and load `.trees` files). Thanks to the msprime and kastore developers for this code, and to Peter Ralph and Jared Galloway for contributing code to SLiM to integrate it with these software packages. The msprime package is licensed under the GPL, and is available at https://github.com/tskit-dev/msprime. The kastore package is MIT licensed and available at https://github.com/tskit-dev/.

27.4 Boost

SLiM contains modified code from Boost (for a smart pointer implementation), which is licensed under the Boost Software License version 1.0 (http://www.boost.org/LICENSE_1_0.txt). The Boost Software License is compatible with the GPL, allowing its use here. Thanks to all of the authors of Boost for their very useful software, which can be downloaded in its full form from their website at http://www.boost.org/users/download/#live. Thanks especially to Peter Dimov, who appears to be the author of the class in question.

27.5 MT19937-64

SLiM contains a 64-bit Mersenne Twister implementation (a random number generator) by Takuji Nishimura and Makoto Matsumoto; thanks to them for this code, which was obtained from http://www.math.sci.hiroshima-u.ac.jp/~m-mat/MT/VERSIONS/C-LANG/mt19937-64.c. Following the terms of their license, the following text is provided from them:

27.6 WiggleTools

SLiM contains code from WiggleTools to perform *t*-tests. WiggleTools is licensed under the Apache 2.0 license (http://www.apache.org/licenses/LICENSE-2.0), which is compatible with the GPL, allowing its use here. Thanks to EMBL-European Bioinformatics Institute for making this code available.

27.7 ObjectPool

SLiM contains a modified version of a C++ object pool class published by Paulo Zemek at http://www.codeproject.com/Articles/746630/O-Object-Pool-in-Cplusplus. His code is under the Code Project Open License (CPOL), available at http://www.codeproject.com/info/cpol10.aspx. The CPOL is not compatible with the GPL. Paulo Zemek has explicitly granted permission for his code to be used in Eidos and SLiM, and thus placed under the GPL as an alternative license. An email granting this permission has been archived and can be provided upon request. This code is therefore now under the same GPL license as the rest of SLiM and Eidos, as stated above.

27.8 Exact summation

SLiM contains modified (translated to C from Python) code to compute the exact summation (within available precision limits) of a vector of floating-point numbers. This code is adapted from Python's `fsum()` function, as implemented in the file `mathmodule.c` in the `math_fsum()` C function, from Python version 3.6.2, downloaded from https://www.python.org/getit/source/. The authors of that code appear to be Raymond Hettinger and Mark Dickinson; thanks to them. The PSF open-source license for Python 3.6.2, which the PSF states is GSL-compatible, may be found on their website at https://docs.python.org/3.6/license.html.

27.9 JSON for Modern C++

SLiM contains code from the JSON for Modern C++ project (https://github.com/nlohmann/json). Diffs from a pull request (https://github.com/nlohmann/json/pull/212) from Henry Schreiner (i.e., not the pull request's diffs, but his diffs in the discussion) have been applied to allow the class to compile under GCC 4.8.x; otherwise the code is unmodified. Thanks to Niels Lohmann, Henry Schreiner, and other contributors for this very useful library. This code is under the MIT license, and is governed by the following notice:

27.10 Other contributions

Smaller snippets of code have been gleaned from the web, particularly from stackoverflow. Credit is given in the SLiM source code where this has occurred, and in all cases the code is licensed under terms compatible with the GSL (as far as we, who are not lawyers, can tell). Thanks to everyone whose code has found its way into SLiM.

28. References

Ayala, F.J., and Campbell, C. (1974). Frequency-dependent selection. *Annual Review of Ecology, Evolution, and Systematics 5*, 115–138.

Boost. (2015). Boost C++ Libraries [version 1.59.0]. URL: http://www.boost.org

Charlesworth, B., Morgan, M.T., and Charlesworth, D. (1993). The effect of deleterious mutations on neutral molecular variation. *Genetics 134*(4), 1289–1303.

Chen, J.-M., Cooper, D.N., Chuzhanova, N., Férec, C., and Patrinos, G.P. (2007). Gene conversion: Mechanisms, evolution and human disease. *Nature Reviews Genetics 8*(10), 762–775.

Comeron, J.M., Ratnappan, R., and Bailin, S. (2012). The many landscapes of recombination in *Drosophila melanogaster*. *PLoS Genetics 8*(10), e1002905.

Dawkins, R. (1976). *The Selfish Gene*. Oxford University Press.

Deutsch, M., and Long, M. (1999). Intron–exon structures of eukaryotic model organisms. *Nucleic Acids Research 27*(15), 3219–3228.

Dieckmann, U., and Doebeli, M. (1999). On the origin of species by sympatric speciation. *Nature 400*(6742), 354–357.

Doebeli, M., and Dieckmann, U. (2003). Speciation along environmental gradients. *Nature 421*(6920), 259–264.

Doudna, J.A., and Charpentier, E. (2014). The new frontier of genome engineering with CRISPR- Cas9. *Science 346*(6213), 1258096-1–1258096-9.

Elyashiv, E., Sattath, S., Hu, T. T., Strutsovsky, A., McVicker, G., Andolfatto, P., Coop, G. & Sella, G. (2016). A genomic map of the effects of linked selection in *Drosophila*. *PLoS Genetics 12*(8), e1006130.

Fiston-Lavier, A.S., and Petrov, D.A. (2013). *Drosophila melanogaster* recombination rate calculator. URL: http://petrov.stanford.edu/cgi-bin/recombination-rates_updateR5.pl. *Drosophila* chromosome map URL: http://petrov.stanford.edu/RRC_scripts/RRCv2.3.tar.gz

Galassi, M., Davies, J., Theiler, J., Gough, B., Jungman, G., Alken, P., Booth, M., and Rossi, F. (2009). GNU Scientific Library Reference Manual [3rd Ed.]. ISBN 0954612078.

Galtier, N., Piganeau, G., Mouchiroud, D., and Duret, L. (2001). GC-content evolution in mammalian genomes: The biased gene conversion hypothesis. *Genetics 159*(2), 907–911.

Gravel, S., Henn, B.M., Gutenkunst, R.N., Indap, A.R., Marth, G.T., Clark, A.G., Yu, F., Gibbs, R.A., Bustamante, C.D., Altshuler, D.L., and Durbin, R.M. (2011). Demographic history and rare allele sharing among human populations. *PNAS 108*(29), 11983–11988.

Grimm, V. (2002.) Visual debugging: A way of analyzing, understanding and communicating bottom-up simulation models in ecology. *Natural Resource Modeling 15*(1): 23–38.

Haller, B.C. (2016). Eidos: A Simple Scripting Language. URL: http://messerlab.org/slim/

Haller, B.C., and Hendry, A.P. (2013). Solving the paradox of stasis: Squashed stabilizing selection and the limits of detection. *Evolution 68*(2), 483–500.

Haller, B.C., Mazzucco, R., and Dieckmann, U. (2013). Evolutionary branching in complex landscapes. *American Naturalist 182*(4), E127–E141.

Hamilton, W.D. (1964a). The genetical evolution of social behaviour I. *Journal of Theoretical Biology 7*(1), 1–16.

Hamilton, W.D. (1964b). The genetical evolution of social behaviour II. *Journal of Theoretical Biology 7*(1), 17–52.

Hill, W. G., and Robertson, A. (1966). The effect of linkage on limits to artificial selection. *Genetical Research 8*(3), 269–294.

Hudson, R.R. (1994). How can the low levels of DNA sequence variation in regions of the *Drosophila* genome with low recombination rates be explained? *PNAS 91*(15), 6815–6818.

Kelleher, J., Etheridge, A.M., and McVean, G. (2016). Efficient coalescent simulation and genealogical analysis for large sample sizes. *PLoS Computational Biology 12*(5): e1004842.

Kelleher, J., Thornton, K.R., Ashander, J., and Ralph, P.L. (2018). Efficient pedigree recording for fast population genetics simulation. *bioRxiv* 248500. DOI: https://doi.org/10.1101/248500

Kimura, M. (1962). On the probability of fixation of mutant genes in a population. *Genetics 47*(6), 713–719.

Leimar, O., Doebeli, M., and Dieckmann, U. (2008). Evolution of phenotypic clusters through competition and local adaptation along an environmental gradient. *Evolution 62*(4), 807–822.

Messer, P.W. (2013). SLiM: Simulating evolution with selection and linkage. *Genetics 194*(4), 1037–1039.

Messer, P.W., and Petrov, D.A. (2013). Population genomics of rapid adaptation by soft selective sweeps. *Trends In Ecology & Evolution 28*(1), 659–669.

Newbigin, E., Anderson, M.A., and Clarke, A.E. (1993). Gametophytic self-incompatibility systems. *The Plant Cell 5*(10), 1315–1324.

Payne, J.L., Mazzucco, R., and Dieckmann, U. (2011). The evolution of conditional dispersal and reproductive isolation along environmental gradients. *Journal of Theoretical Biology 273*(1), 147–155.

Philipps, P.C. (2008). Epistasis – the essential role of gene interactions in the structure and evolution of genetic systems. *Nature Reviews Genetics 9*(11), 855–867.

R Core Team. (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL: https://www.R-project.org/

Ratnakumar, A., Mousset, S., Glémin, S., Berglund, J., Galtier, N., Duret, L., and Webster, M.T. (2010). Detecting positive selection within genomes: The problem of biased gene conversion. *Philosophical Transactions of the Royal Society B 365*(1552), 2571–2580.

Sattath, S., Elyashiv, E., Kolodny, O., Rinott, Y., and Sella, G. (2011). Pervasive adaptive protein evolution apparent in diversity patterns around amino acid substitutions in *Drosophila simulans*. *PLoS Genetics 7*(2), e1001302.

Servedio, M.R., Van Doorn, G.S., Kopp, M., Frame, A.M., and Nosil, P. (2011). Magic traits in speciation: 'Magic' but not rare?. *Trends in Ecology & Evolution 26*(8), 389–397.

Smith, J.M., and Haigh, J. (1974). The hitch-hiking effect of a favorable gene. *Genetical Research 23*(1), 23–25.

Vincenot, C.E., Carteni, F., Mazzoleni, S., Rietkerk, M., and Giannino, F. (2016). Spatial Self-Organization of Vegetation Subject to Climatic Stress—Insights from a System Dynamics—Individual-Based Hybrid Model. *Frontiers in Plant Science 7*, 636.